

AWARD NUMBER: W81XWH-08-1-0484

TITLE: "NEW HEART FAILURE TREATMENT CAPABILITY FOR REMOTE ENVIRONMENTS"

PRINCIPAL INVESTIGATOR:

DR. MARK P. ANSTADT, M.D.

CONTRACTING ORGANIZATION:

LIFEBRIDGE TECHNOLOGIES, LLC  
DAYTON, OHIO 45409

REPORT DATE: June 2013

TYPE OF REPORT: FINAL

PREPARED FOR:

U.S. Army Medical Research and Materiel Command  
Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT: Approved for Public Release;  
Distribution Unlimited

The views, opinions and/or findings contained in this report are those of the author(s) and should not be construed as an official Department of the Army position, policy or decision unless so designated by other documentation.

# REPORT DOCUMENTATION PAGE

*Form Approved*  
OMB No. 0704-0188

Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing this collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to Department of Defense, Washington Headquarters Services, Directorate for Information Operations and Reports (0704-0188), 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202-4302. Respondents should be aware that notwithstanding any other provision of law, no person shall be subject to any penalty for failing to comply with a collection of information if it does not display a currently valid OMB control number. PLEASE DO NOT RETURN YOUR FORM TO THE ABOVE ADDRESS.

<b>REPORT DOCUMENTATION PAGE</b>			<i>Form Approved</i> OMB No. 0704-0188	
Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing this collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to Department of Defense, Washington Headquarters Services, Directorate for Information Operations and Reports (0704-0188), 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202-4302. Respondents should be aware that notwithstanding any other provision of law, no person shall be subject to any penalty for failing to comply with a collection of information if it does not display a currently valid OMB control number. PLEASE DO NOT RETURN YOUR FORM TO THE ABOVE ADDRESS.				
1. REPORT DATE June 2013		2. REPORT TYPE FINAL		3. DATES COVERED 14Jul2008 - 19May2012
4. TITLE AND SUBTITLE NEW HEART FAILURE TREATMENT CAPABILITY FOR REMOTE ENVIRONMENTS		5a. CONTRACT NUMBER W81XWH-08-1-0484		5b. GRANT NUMBER
		5c. PROGRAM ELEMENT NUMBER		5d. PROJECT NUMBER
		5e. TASK NUMBER		5f. WORK UNIT NUMBER
6. AUTHOR(S) 1. DR. MARK P. ANSTADT, M.D., PRINCIPAL INVESTIGATOR 2. DR. DAVID B. REYNOLDS, PhD., Co-PRINCIPAL INVESTIGATOR  E-Mail: <a href="mailto:MPANSTADT@AOL.COM">MPANSTADT@AOL.COM</a> <a href="mailto:beckydarnier@yahoo.com">beckydarnier@yahoo.com</a>		8. PERFORMING ORGANIZATION REPORT NUMBER		
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) LIFEBRIDGE TECHNOLOGIES, LLC 30 EAST APPLE STREET, SUITE 6252 DAYTON, OHIO 45409		9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES) U.S. Army Medical Research and Material Command Fort Detrick, Maryland 21702-5012		
10. SPONSOR/MONITOR'S ACRONYM(S)		11. SPONSOR/MONITOR'S REPORT NUMBER(S)		
12. DISTRIBUTION / AVAILABILITY STATEMENT  Approved for Public Release; Distribution Unlimited				
13. SUPPLEMENTARY NOTES				
14. ABSTRACT The FINAL annual report summarizes the salient background information and the successful completion of the proposed project with emphasis on accomplishments from 5/20/2012 to 5/19/2013. The purpose of this project was to develop a device for rapid, effective, circulatory support for remote areas. Direct mechanical ventricular actuation (DMVA) is a non-blood contacting method that can re-establish normal hemodynamics in the fibrillating (non-beating) and severely failing heart within minutes. This project's objective was to develop a portable, compact, user-friendly DMVA drive system for simplified operation. Proven, pre-existing DMVA drives were used for verifying the new drive met functional requirements. Project objectives were to develop a manual powered hand pump (HP), define optimal HP operation, design a motorized drive to power the prototype pump, and then use these inputs to construct the automated, prototype drive. In-vivo testing utilized a dedicated data acquisition system integrated with inputs selected to best interrogate the drive system's functionality and related physiologic effects. Thereby, the HP integrated with a prototype linear drive was been evaluated and reduced to a compact, automated drive (AD). The final prototype DMVA drive system was successfully constructed and tested. In-vitro bench testing on a custom mock circulatory loop (MCL) allowed final modifications to be made prior to verifying the system's functionality with in-vivo animal testing. The AD incorporates a removable HP which enables temporary acute support in the event of power failure. Final in-vitro and in-vivo testing verified the new system achieved functionality equivalent to pre-existing drive systems while providing a portable, AD useful for remote areas.				
15. SUBJECT TERMS DIRECT MECHANICAL VENTRICULAR ACTUATION, CIRCULATORY SUPPORT, HEART FAILURE, DRIVE SYSTEM				
16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT UU	18. NUMBER OF PAGES 63
a. REPORT U	b. ABSTRACT U	c. THIS PAGE U	19a. NAME OF RESPONSIBLE PERSON USAMRMC	
			19b. TELEPHONE NUMBER (include area code)	

## Table of Contents

	<u>Page</u>
<b>1. Introduction.....</b>	<b>4</b>
<b>2. Keywords.....</b>	<b>4</b>
<b>3. Overall Project Summary.....</b>	<b>4-15</b>
<b>4. Key Research Accomplishments.....</b>	<b>15</b>
• <b>DMVA Background, Salient Aspects, Future Goals.....</b>	<b>16-35</b>
<b>5. Conclusion.....</b>	<b>35</b>
<b>6. Publications, Abstracts, and Presentations.....</b>	<b>36</b>
<b>7. Inventions, Patents and Licenses.....</b>	<b>36</b>
<b>8. Reportable Outcomes.....</b>	<b>37-45</b>
<b>9. Other Achievements.....</b>	<b>46</b>
<b>10. References.....</b>	<b>46-47</b>
<b>11. Appendices.....</b>	<b>47-63</b>

## 1. INTRODUCTION

This final annual report summarized all key project goals completed to date and includes pertinent background information that justified the project. The purpose of this project was to develop a device for rapid, effective, circulatory support in remote areas. DMVA has already demonstrated its potential for providing resuscitative circulatory support with particularly relevant attributes including technically simply installation, rapid return and maintenance of perfusion to vital organs and the absence of any blood contact. This unique method of non-blood contacting biventricular support that was first described by George L. Anstadt, DVM. The method utilizes a pneumatically powered heart cup to deliver systolic and diastolic forces to the surface of the ventricular myocardium. DMVA has proven to be effective in providing total circulatory support to the fibrillating, or severely failing heart. This report summarizes background information pertinent to the development of DMVA and other related non-blood contacting circulatory support technologies. The background explains DMVA's unique life-saving attributes, enabling a better appreciation for the significance of the project. The report will then cover salient aspects pertaining to the project and its completion. Finally, future goals will be outlined for clinical use of the developed technology.

## 2. KEYWORDS

1. DMVA – DIRECT MECHANICAL VENTRICULAR ACTUATION
2. HP – HAND PUMP
3. AD – AUTOMATED DRIVE
4. MCL – MOCK CIRCULATORY LOOP
5. ECHO - ECHOCARDIOGRAPHIC
6. DCC – DIRECT CARDIAC COMPRESSION
7. RV – RIGHT VENTRICLE
8. LV – LEFT VENTRICLE
9. CPB – CARDIOPULMONARY BYPASS
10. TEE – TRANSESOPHAGEAL
11. ST – SWITCHED TANK

## 3. OVERALL PROJECT SUMMARY

This report represents the FOURTH AND LAST annual report for Contract # W81XWH-08-1-0484T. The original start date for this contract was 7/14/2008. However, no activity occurred until the grant was transferred to LifeBridge Technologies, LLC, with an approved start date of 5/20/2009 from USAMRAA. Our FIRST THREE annual reports reviewed activities from 5/20/2009 through 5/20/2012. This FOURTH and FINAL report summarizes subsequent project activities beginning in 5/20/2012 until 5/19/2013.

This final annual report summarized all key project goals completed to date and includes pertinent background information that justified the project. The project is further developing DMVA for use in remote areas. DMVA is a non-blood contacting method of resuscitation for support of the arrested, or severely failing heart. The project's principle goal is to develop a portable, compact, user-friendly drive system that does not require significant expertise for operation of the unit.

All proposed milestones have now been completed. Those milestones completed prior to this final report include:

- (1) In-vivo studies to derive drive dynamics and pneumatic piston modifications.
- (2) Design and fabrication of the HP.
- (3) Design for integrating the HP into the automated system.
- (4) Assembly of the prototype MCL for bench testing.
- (5) Design and fabrication of the initial AD prototype.
- (6) Modifications of the AD prototype system based on in-vivo testing.
- (7) Final design of the AD prototype system.
- (8) Fabrication/initial assembly of the automated volume regulated drive system prototype.

Milestones completed since the last quarterly report include:

- (9) Analysis of interface/control and manual HP features.
- (10) Final modifications of automated VRD prototype.
- (11) Final testing of automated VRD prototype.

**Report of Financials:**

The table below summarizes the utilization of financials during the first year of the funded project period.

**YEAR END FINANCIALS:**

**5/20/2012 – 5/19/2013**

STAFF MEMBER	ROLE	% EFFORT-MONTHS 36-48
MARK P ANSTADT	PI	37.6
REBECCA DARNER	RESEARCH COORDINATOR	38.8
ANTHONY PEREZ-TAMAYO	CONSULTANT	<1
JENNIE GALLIMORE	STATISTICIAN	<1
PETER SCHIFF	LEAD ENGINEER	3
RICHARD LESLEY	ENGINEERING TECHNICIAN	23.9
KELLY SWARTZMILLER	TECHNICAL ASSISTANT	<1
NICK GARVIN	TECHNICAL ASSISTANT	8.4
MEGAN MARKL	TECHNICAL ASSISTANT	3.9
SABRINA METZGER	TECHNICAL ASSISTANT	34.6
KEVIN CARNAHAN	TECHNICAL ASSISTANT	34.6

**Contract expenditures to date:**

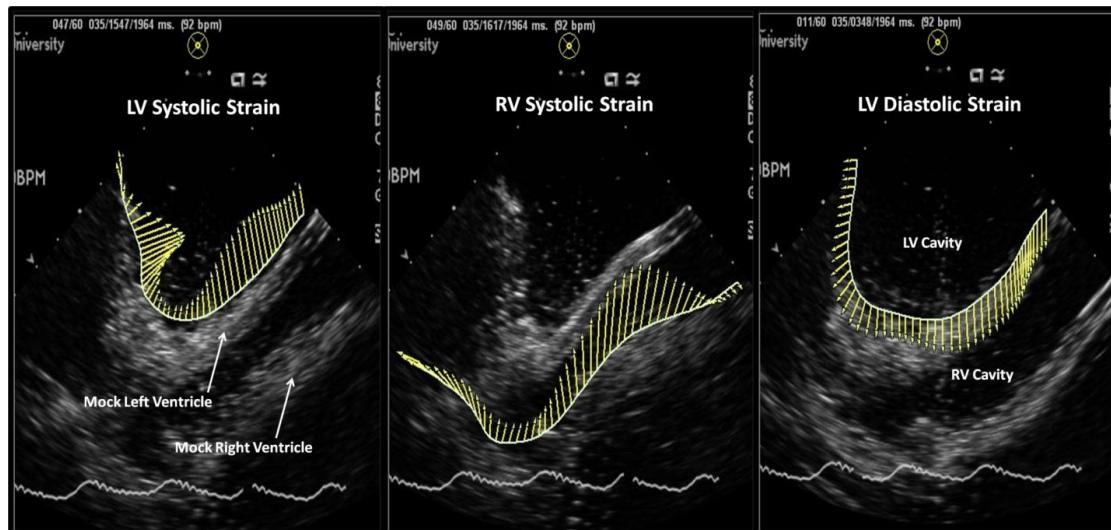
COST ELEMENTS	THIS QUARTER	CUMULATIVE
Personnel	\$15,762	\$160,512
Fringe Benefits	0.00	0.00
Supplies	0.00	0.00
Equipment	79,197.62	203,125.25
Travel	0.00	9,774.09
Other Direct Costs	28,001.23	269,631.83
<b>Subtotal</b>	<b>\$122,960.85</b>	<b>\$645,206.02</b>
Indirect Costs	\$23,703.35	\$151,919.80

Fee	0.00	0.00
<b>Total</b>	<b>\$146,664.22</b>	<b>\$849,717.63</b>

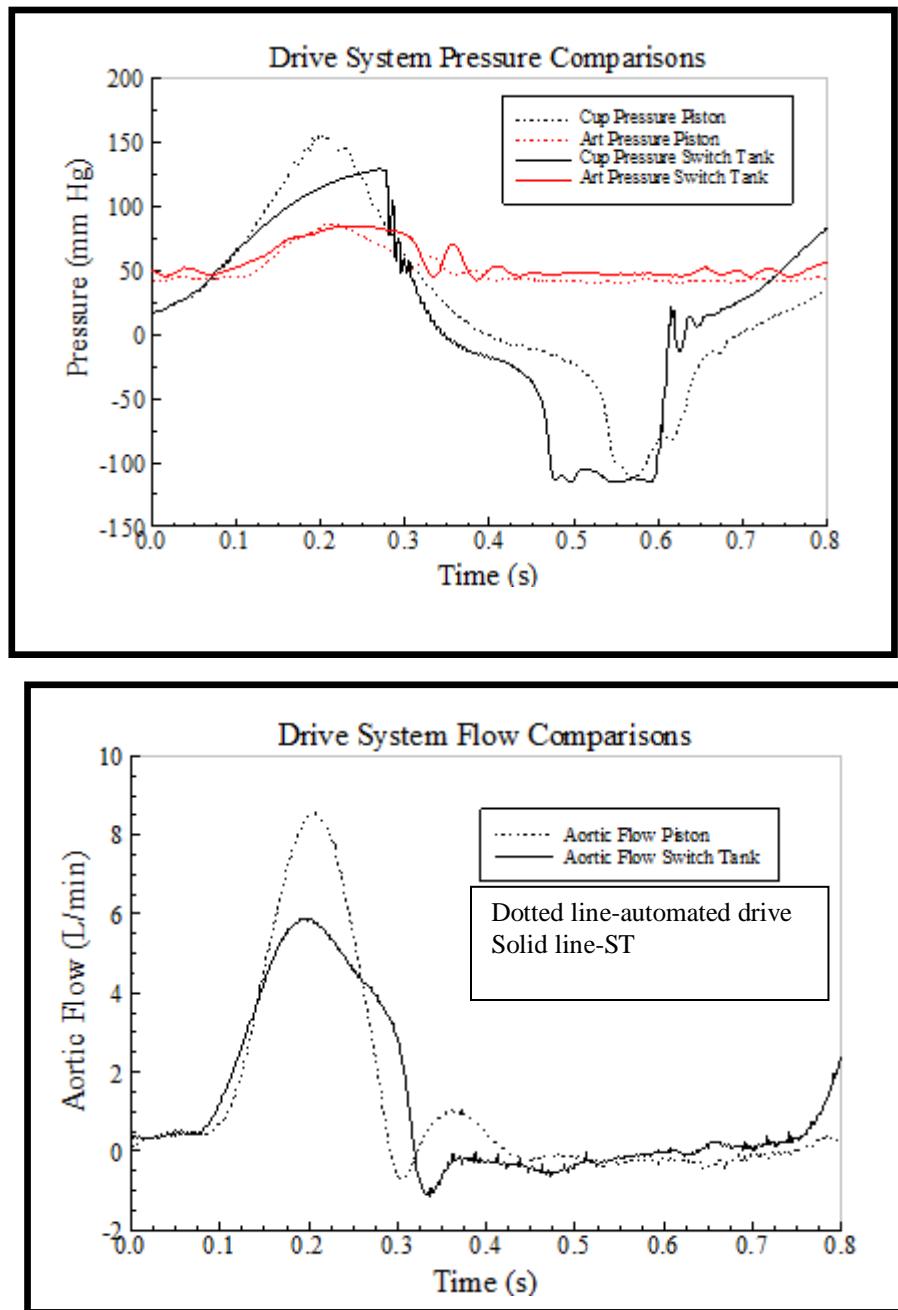
A novel, custom MCL was used to verify functionality of the drive before completing animal testing:



Echocardiographic (ECHO) interrogation of the mock ventricles was included in the analysis to verify functionality:  
Below are ECHO images of Mock Ventricles actuated by the AD system:

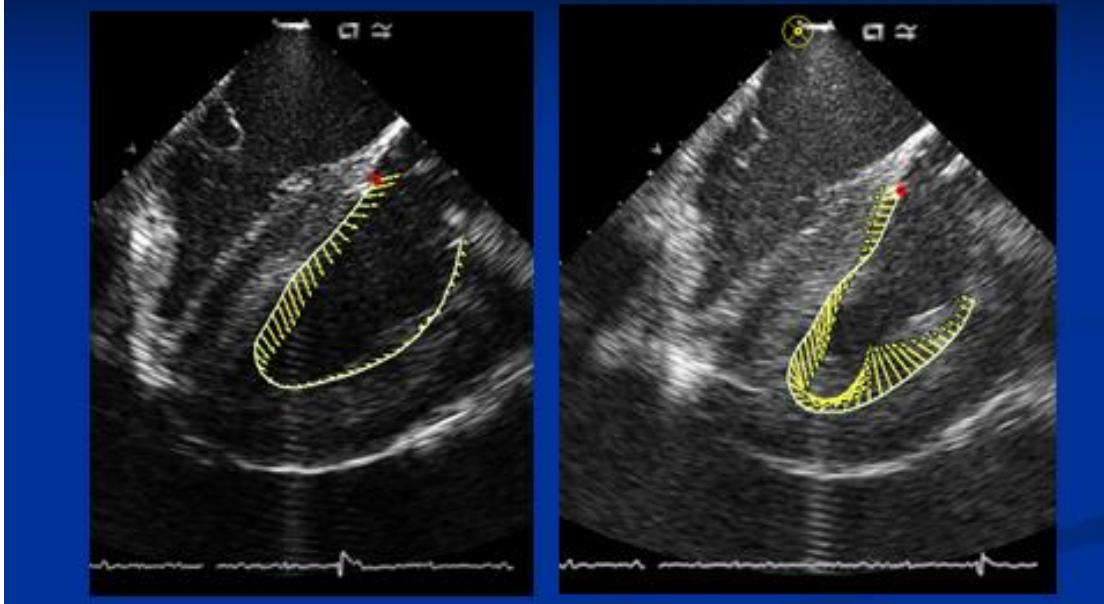


Data was compared between the switched tank (ST) and the prototype drives to verify equivalence.

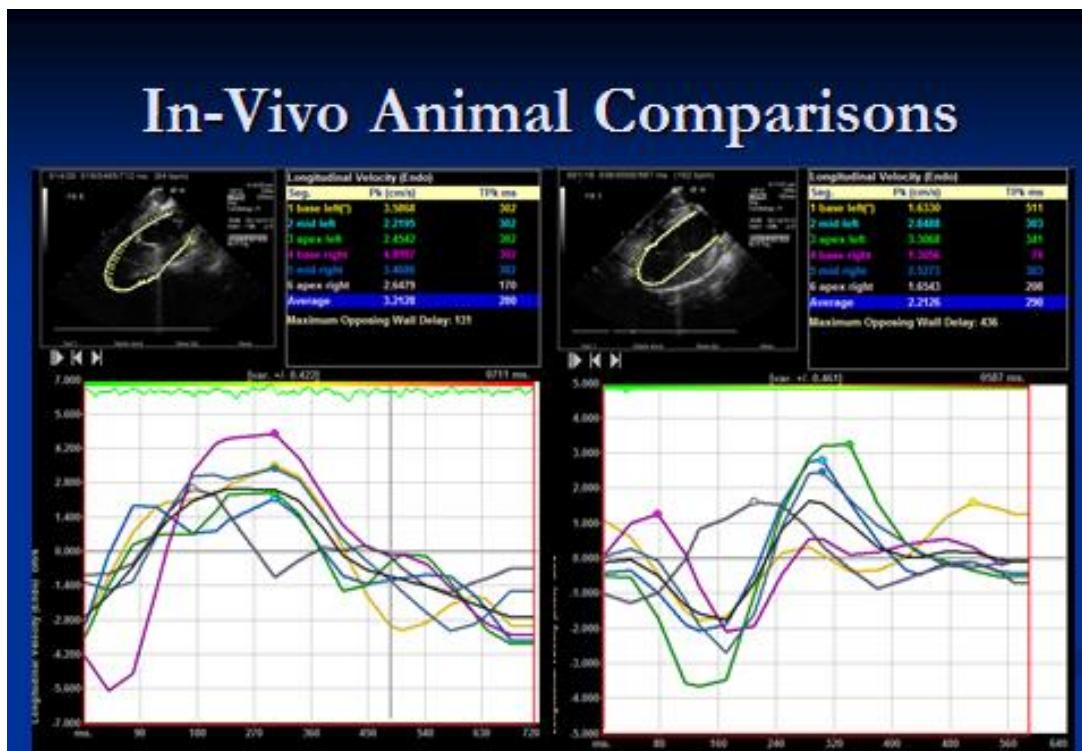


Comparisons were then made between the AD and the ST system in animals using a similar experimental algorithm. Below is an example ECHO image during DMVA support using the automated, piston drive system (left, in systolic actuation/compression) and ST system (right, during diastolic actuation) during support of the fibrillating heart:

# In-Vivo Animal Evaluations



Below are strain analysis examples of DMVA support using the automated, piston drive system (left) and the ST system (right) during support of the severely failing heart.



Data from these in-vivo experimental comparisons were averaged and mean values are provided in the below tables and graphs (piston= AD):

Drive System Mock Comparisons				
Drive System	Max Cup Pressure (mm Hg)	Min Cup Pressure (mm Hg)	Integral Cup Pos Pressure (mm Hg*s)	Integral Cup Neg Pressure (mm Hg*s)
Piston	143.3	-104.0	49.3	-15.9
Switch Tank	118.4	-103.4	44.8	-27.2

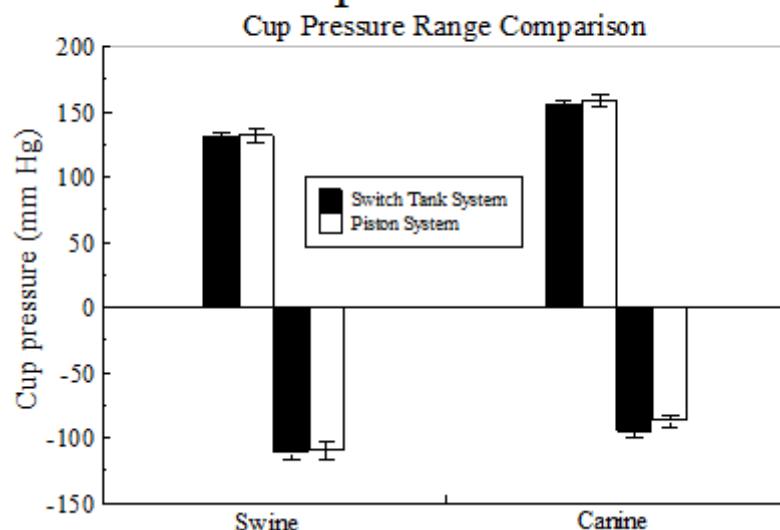
Drive System	Max LV Pressure (mm Hg)	Max RV Pressure (mm Hg)	Mean LA Pressure (mm Hg)	Mean RA Pressure (mm Hg)
Piston	98.6	103.6	18.1	9.1
Switch Tank	93.5	95.5	18.1	9.0

Drive System Mock Comparisons						
Drive System	MAP (mm Hg)	Max Arterial Pressure (mm Hg)	Min Arterial Pressure (mm Hg)	Mean Pulmonary Pressure (mm Hg)	Max Pulmonary Pressure (mm Hg)	Min Pulmonary Pressure (mm Hg)
Piston	79.3	96.8	67.4	39.2	56.3	23.3
Switch Tank	75.1	86.8	65.4	39.1	53.6	26.2

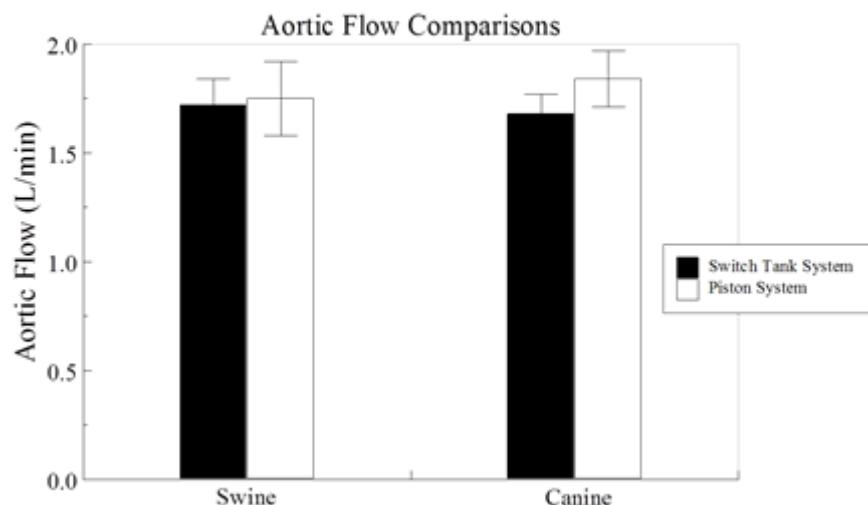
  

Drive System	Max Aortic Flow (L/min)	Average Aortic Flow (L/min)	Average Pulmonary Flow (L/min)	LV Stroke Volume (ml)	RV Stroke Volume (ml)
Piston	7.38	1.36	3.98	31.3	94.7
Switch Tank	4.45	1.31	4.15	33.3	99.4

## In-Vivo Cup Pressure Comparisons

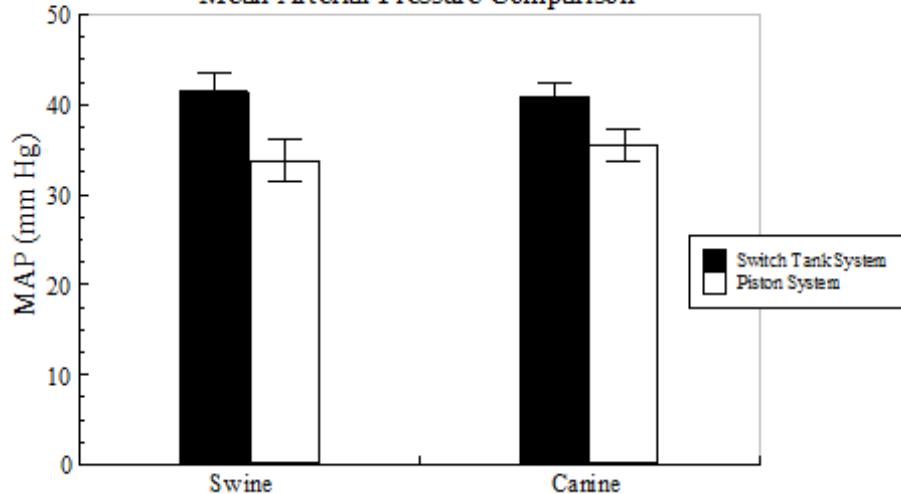


## In-Vivo Cardiac Output Comparisons



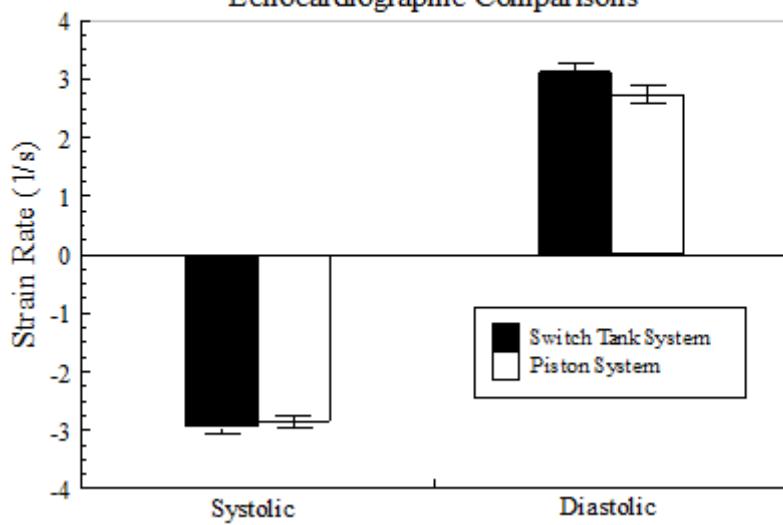
## In-Vivo MAP Comparisons

Mean Arterial Pressure Comparison



## In-Vivo Strain Rate Comparisons

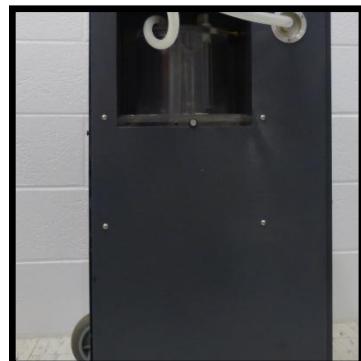
Echocardiographic Comparisons



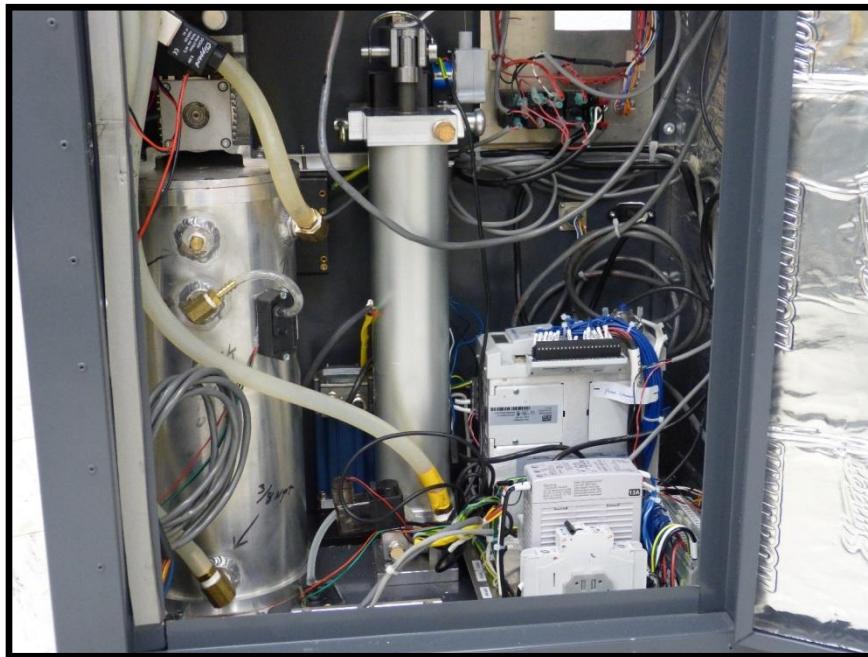
Below are pictures of the final automated, piston drive showing its housing and portable dolly features:



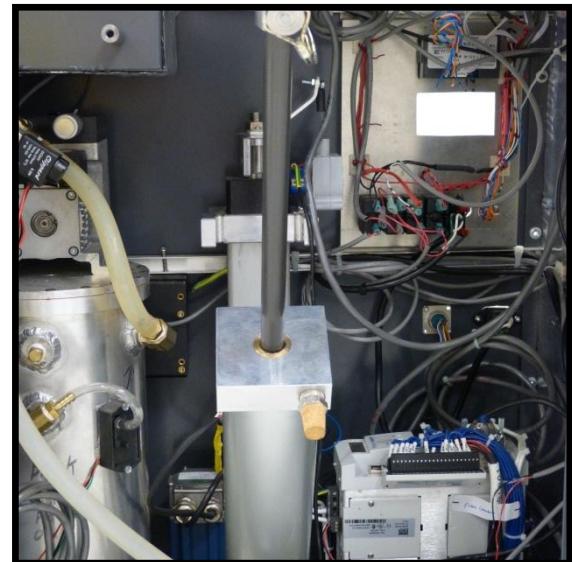
Below is an illustration showing DMVA cup attachment to the DMVA AD:



Below is a view of the internal integration of the piston and automated components:



Below is an illustration of the HP being actuated during manual operation of the AD:



The AD system was then bench tested using the MCL support system to verify functionality for cup sizes 80 thru 130. The results demonstrated the system could perform at the pre-selected drive rates with adequate actuation of DMVA cups for resuscitation in this wide range of clinically relevant heart sizes.

Future efforts will focus on reducing the current drive to an even smaller scale for use in remote areas in the field of resuscitative circulatory support and bridging to other devices.

## STATEMENT OF WORK

The primary objective of this project pertains to the design and fabrication of a portable VRD for DMVA utilization in remote areas. Performance objectives were outlined with pertinent deliverables and milestones for this project. These outlined deliverables and milestones were arranged in a timeline. Therefore, achieving each consecutive milestone would provide needed conditions to proceed to the subsequent project objectives.

**Year 1:** A total of ten canine experiments will be performed, with a goal of six successful experiments for data analysis. Mock-loop studies will be conducted after each canine experiment, establishing the prototype drive test parameters. During the next two or three months the initial prototype design will be finalized based on specifications collected from the breadboard. Fabrication of the prototype will occur during the last six months of the year. Mock-loop testing on the prototype will begin near the end of the manufacturing in the last month of the year.

***Key deliverables for year 1:***

- 1) Completion of Breadboard In-Vivo Canine Study.
- 2) Completion of Breadboard In-Vitro Mock-Loop studies to establish.
- 3) Design of Prototype I.
- 4) Construction of First Prototype drive.
- 5) Initiation of Mock-Loop testing of First Prototype.
- 6) Completion and verification of appropriate documentation.

***Year 1 Milestones:***

- 1) Complete Breadboard In-Vivo & Mock-Loop studies.
- 2) Complete design and fabrication of First Prototype drive.

**Year 2:** The first four months will be devoted to testing and modifying the prototype drive based on in-vitro and in-vivo testing. Mock-loop testing will finish in the first month of the year, to be followed by two to three in-vivo prototype studies. Based on in-vivo experimental data, the prototype will be modified. In-vitro testing will be conducted with the mock-loop near the end of modification to access the viability of the altered prototype model. The repeated process of in-vivo testing, prototype modifications and in-vitro testing, with 1-3 iterations likely, will lead to the development of the final prototype design and final design specifications by the end of year two.

***Key deliverables for year 2:***

- 1) Successful completion of mock-loop and in-vivo testing of First Prototype drive.
- 2) Modify Prototype as determined by mock and animal testing results (2-3 revisions).
- 3) Finalization of Prototype drive design.
- 4) Completion and verification of appropriate documentation.

***Year 2 Milestones:***

- 1) Perform in-vitro and in-vivo testing of prototypes.
- 2) Arrive at Final Design Prototype.

**Year 3:** In the first four months, six successful in-vivo experiments will be performed on the final design prototype to analyze its effectiveness. Final adjustments in the drive control system will be made in the first two or three animals. Analyses will be performed by an independent clinical investigator to assess user-friendliness and functionality. In the next two months, training algorithms will be developed prior to pre-clinical testing. In the final six months the final design prototype will undergo pre-clinical testing under an independent clinical direction. A total of six successful experiments will provide data for comparison to breadboard results obtained in year one to test the study hypothesis with a focus of developing a protocol for clinical trials.

**Key Deliverables for year 3:**

- 1) In-Vivo Final Design Prototype study.
- 2) Final control interface modifications of Final Design Prototype.
- 3) Establishment of training protocol.
- 4) Pre-clinical testing of Final Design Prototype.
- 5) Data analysis to test study hypothesis.

**Year 3 Milestones:**

- 1) Finalize user-interface/control features of final prototype.
- 2) Complete animal tests using independent clinical investigator.

## **4. KEY RESEARCH ACCOMPLISHMENTS**

Progress during the 16<sup>th</sup> quarter (the final quarter of this project) focused on three critical tasks:

- (1) Analysis of interface/control of the automated VRD prototype and integrated manual HP.
- (2) Completion of final modifications of automated VRD prototype.
- (3) Final testing of automated VRD prototype.

Two automated VRD prototype drive systems were thereby assembled with all necessary modifications to ensure functionality. The two systems were tested on the custom MCL and with in-vivo experiments following the same protocols developed during the project. Use of ultrasound imaging for novel strain analysis provided more robust validation results in both the MCL & in-vivo animal testing. This significantly enhanced the validity of the final testing to demonstrate effective drive performance. Analysis of the final automated VRD prototype demonstrated that the portable, AD system functioned as well as prior existing drive systems as anticipated.

**Objectives completed during the final quarter of the project period**

The final prototype AD system underwent both in-vitro (MC) and in-vitro (animal) testing with comparative analyses with the pre-existing ST system. Two prototype drives were assembled and demonstrated functionality and feasibility. The final portable, automated VRD evaluations with in-vivo experiments and in-vitro MCL testing proved the project hypothesis. All final refinements in the drive control features and user-interface were incorporated into the drive for these final evaluations.

**A. Key Deliverables completed during the final quarter of the project:**

- (1) Assembly of the final portable automated VRD with all necessary modifications
- (2) In-vivo analysis of user-interface and control, HP assembly and user-interface
- (3) In-vivo and in-vitro assessment of final prototype for functionality and ease of use
- (4) Data analysis to testing the study hypothesis that the portable, automated VRD drive is equivalent to pre-existing drives

**B. Milestones Completed during the final quarter of the project:**

- (1) Fabrication/assembly of the final automated VRD prototype
- (2) Final testing of VRD verifying its functionality and equivalence to pre-existing DMVA drive systems

**Scientific Progress and Objectives during the 16th quarter (4/01/2013-5/19/2013) is summarized below:**

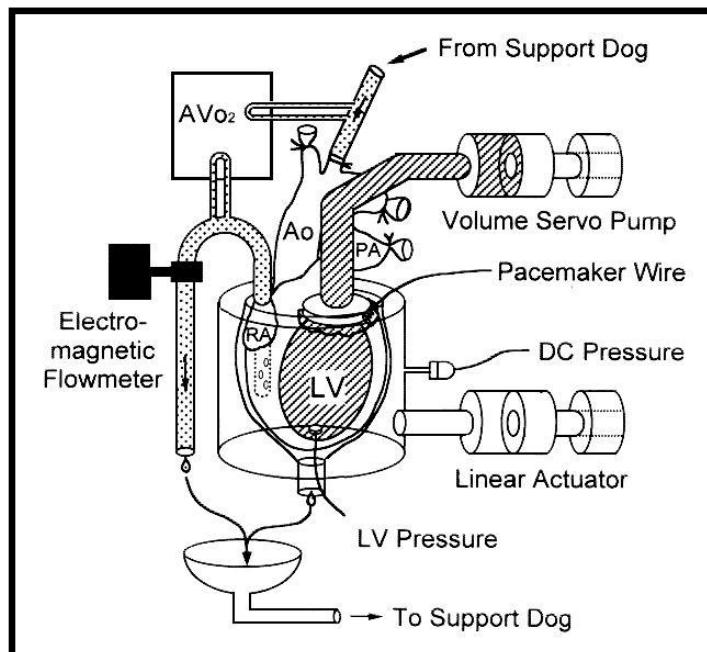
First components for the final automated VRD prototype were assembled in a custom, portable housing. Notably, this final portable, automated VRD was constructed in duplicate. The completed unit was then tested for functionality using both in-vivo, animal experiments as well as bench testing with the MCL. Animal experiments included both canine and swine models. The >50 lb canine is representative of a small human, while the >180 lb swine an average size human. The MCL platform provided a means for verifying functionality under steady-state physiologic loads pertinent to larger human. Testing of the final prototype assessed functionality, control features and user-friendliness. Final modifications were made regarding user-interface and the manual HP to improve these features. Simple training algorithms from intuitive touch-screen directions were used for pre-clinical testing of the final automated VRD prototype. The completed prototype then underwent in-vivo and in-vitro testing comparing it to the prior drive systems.

## DMVA BACKGROUND, SALIENT ASPECTS, AND FUTURE GOALS

The study of how mechanical forces can augment cardiac pump performance has led to a large body of scientific data. These works done investigating DMVA as well as other distinctly different devices. Salient aspects of these prior studies illustrate and justify the value of advancing DMVA technology in the manner proposed by this project. It should be recognized that early work pertaining to DMVA employed rather rudimentary devices. These devices were designed to compress the heart for improving systolic pump function. Devices that compress the ventricles are defined as “direct cardiac compression (DCC)” devices. DCC describes compression of the heart for the purpose of augmenting ventricular systolic pump function. Although DCC is pertinent to DMVA, it is important to understand DCC devices do not provide diastolic assist. In fact, DCC devices generally impair diastolic ventricular function. DMVA distinctly aids diastolic function which is a distinguishing feature pertaining to DMVA’s efficacy.

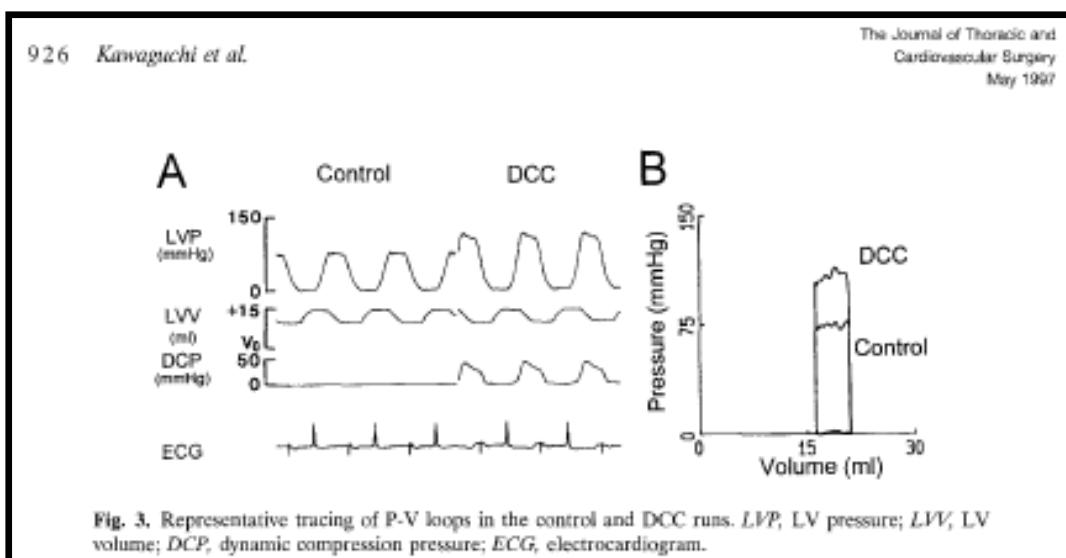
When considering the efficacy of DMVA, one needs to also recognize the implications on the right ventricle (RV). RV function is very vulnerable to the constrictive aspects of any compressive device resulting in compromised filling. This again is where DMVA’s diastolic assist plays a critical role. Therefore, it is also important to appreciate that many DCC investigations focused on the left ventricle (LV). Many times with isolated hearts preparations that excluded any considerations for RV function. Therefore, the very nature of such experiments did not account for the importance of either diastolic function or RV function both of which have implications on the efficacy of DCC.

Early isolated heart preparations utilized for evaluating DCC’s effect on LV function would typically exclude the RV. Chambers were positioned around the outer surface of the heart served as the DCC platform. These cardiac compression chambers could provide variable degrees of DCC. These in-vitro platforms provided estimates of DCC’s potential impact on important physiologic variables such as LV pressure, aortic flow and pressure. Although, such experiments provided fundamental understanding of DCC’s potential effect on LV performance, these in-vitro experiments employed bulky compression devices that could not be directly translated to practical, implantable devices. Furthermore, assessment of the RV function and/or diastolic function were typically excluded which further makes translation of the results to any practical, in-vivo method of cardiac compression limited at best.

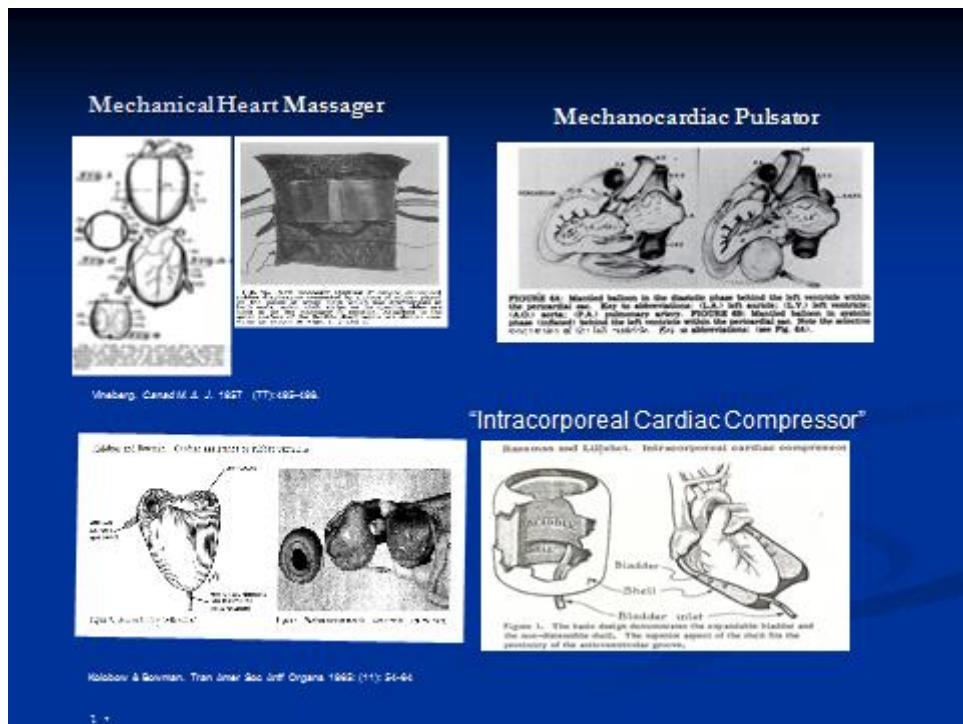


In general, the degree of DCC applied to the left ventricle results in an equal, additive degree of LV pressure generated by the native heart. This principle is pertinent to LV and DCC pressures within the physiologic range. The diagram below illustrates LV pressure in a normal beating, isolated heart before (control) and during (DCC) application of dynamic

compression pressures timed to ventricular systole. Note the DCC pressures were additive to underlying LV pressure during the control state



Given the potential advantages of non-blood contacting circulatory support, a variety of device designs were tested to develop an effective, feasible means for applying DCC in humans. The obvious challenge was creating a device that feasibly fit the heart and effectively aided pump function. A number of devices were designed with these intentions (examples shown below).



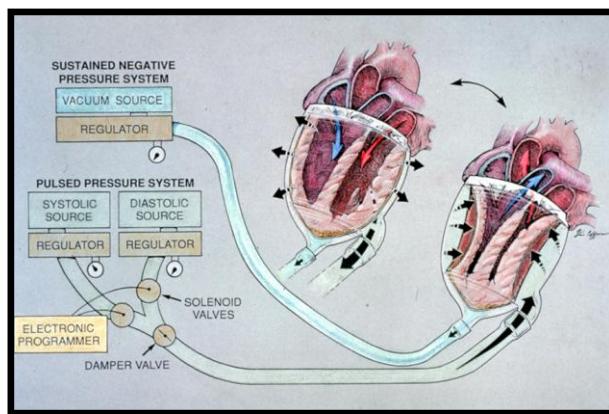
As evident from these illustrations, most of devices were relatively impractical, difficult to install and had little efficacy for providing meaningful cardiac support. Results from laboratory studies using such devices were not particularly convincing and questioned the feasibility of DCC for clinical applications. Importantly, these early devices only provided cardiac compression which only aids systolic function.

George L. Anstadt began work on a unique method of DCC circulatory support which not only compressed the heart, but also aided in ventricular filling or diastolic function. He likened this novel idea to the iron lung which altered atmospheric pressures around the chest to aid in lung ventilation

The first device he built utilized a latex diaphragm molded from casts made of the native heart. The diaphragm was bonded within a rigid Pyrex housing to allow positive and negative pneumatic forces to act on the inner latex diaphragm. The design included an opening in the apex of the housing that allowed vacuum forces to serve as a means for attaching the device non-traumatically to the heart. A picture of the first device is shown below which was successfully used to support the circulation for five hours during ventricular fibrillation.



The device utilized a pneumatic drive system to provide alternating positive and negative forces to the heart cup. An illustration of the drive system and heart cup is shown below:



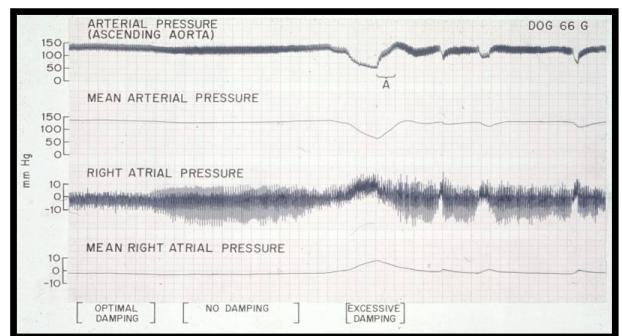
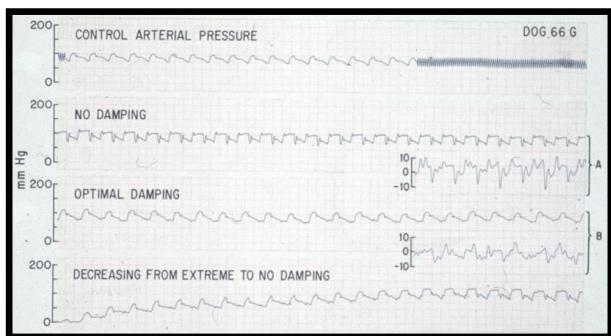
Work with this construct was advanced over the next 15 years with improvements in the design of the outer housing and inner flexible liner.



Using these devices, a pneumatic drive system was developed for controlling the manner in which DMVA actuated the heart. The systems were based on compressors that accumulated positive and negative pressures in tanks which could be switched thru a solenoid valve in a cycle manner. Control of the absolute pressure, rate of actuation and resistance in the

drive lines were the manner in which the operative could modulate the action of DMVA on the heart. A picture of one of these drive systems is shown above:

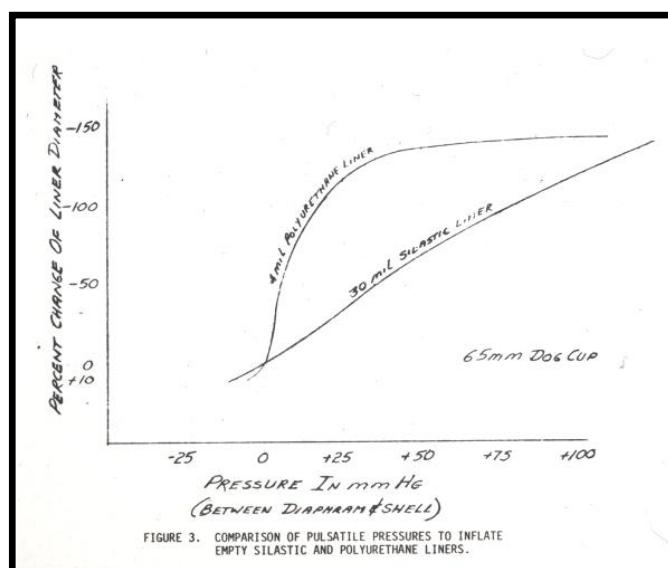
By regulating the “dampening” or resistance in the drive line, the operator could achieve physiologic hemodynamics that mimicked the normal physiologic state as shown below:



Most experiments were done in canine and successful support with long-term survival was achieved in animals receiving DMVA support for days in ventricular fibrillation followed by defibrillation and recovery with normal heart function. The picture below shows an animal awake during DMVA support of the fibrillating heart:

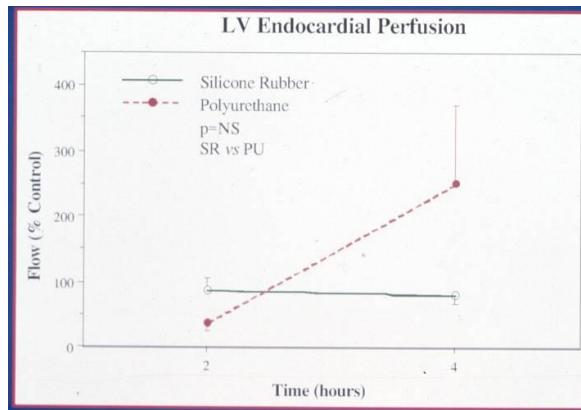


Notable, important differences existed in the characteristics of materials used in DMVA heart cups. Below is a figure illustrating the manner in which silicones versus polyurethanes behave when stretched:

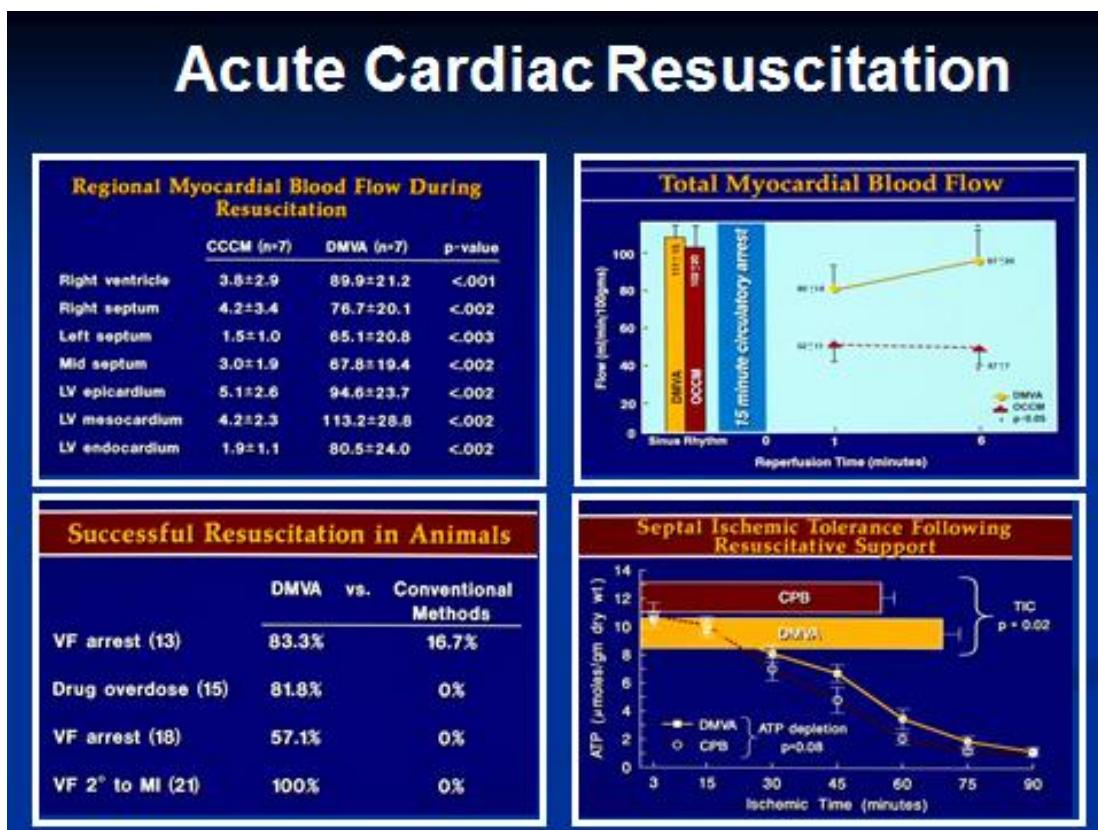


These physical characteristics were fundamentally different. I was discovered that the relatively “isotropic” behavior of silicone rubbers were the most favorable foratraumatic support of the fibrillation heart. When silicone rubber constructed DMVA cups were compared to polyurethane constructed cups, the results were dramatic. Specifically, Silicone rubber

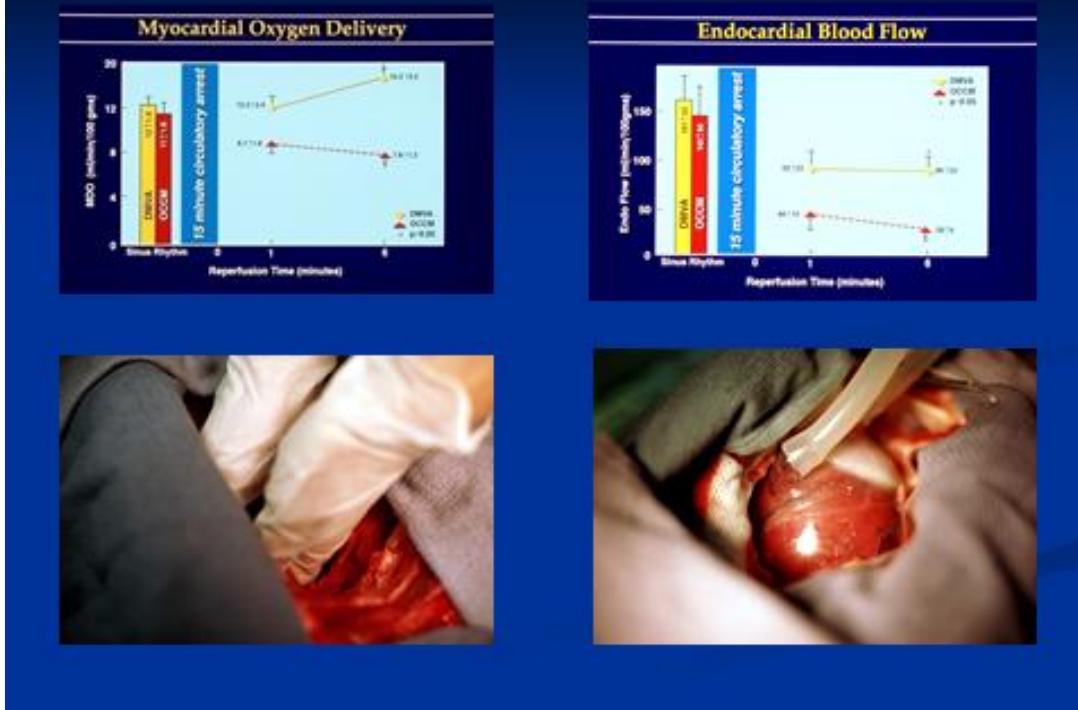
cups resulted in hearts being preserved while the polyurethane constructed devices damaged the myocardium resulting in reduction in ATP stores that mimicked a severely injured heart, probably due to damage of the mitochondria. During support with Polyurethane devices heart became hyperemic as autoregulation led to increased blood flow to the seemingly ischemic myocardium (see graphic below):



The focus with DMVA support centered around resuscitation as the device could be applied rapidly to return the circulation following cardiac arrest or sudden death. Comparisons between DMVA support and conventional methods of cardiac resuscitation such as closed-chest or open chest massage were dramatic (see below):

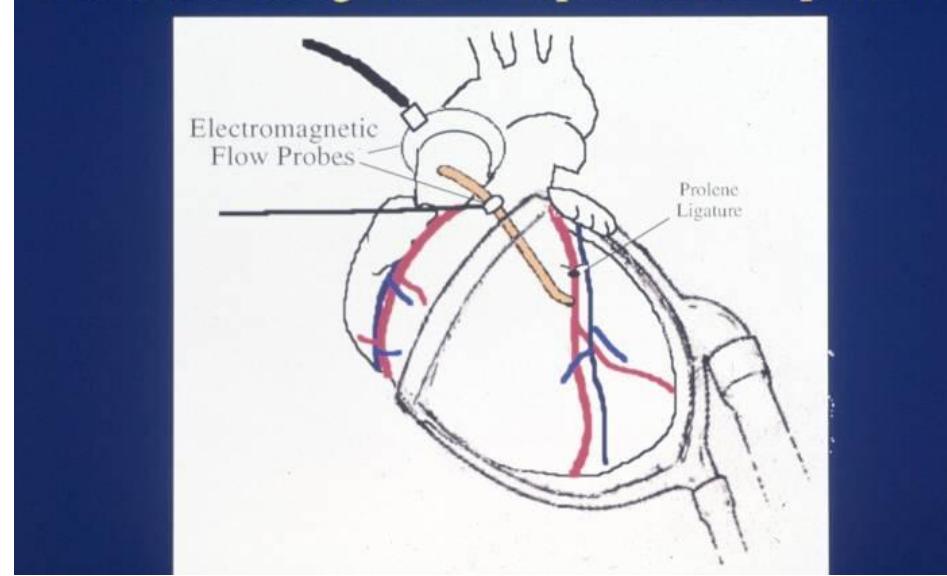


# HAND CARDIAC MASSAGE VS DMVA



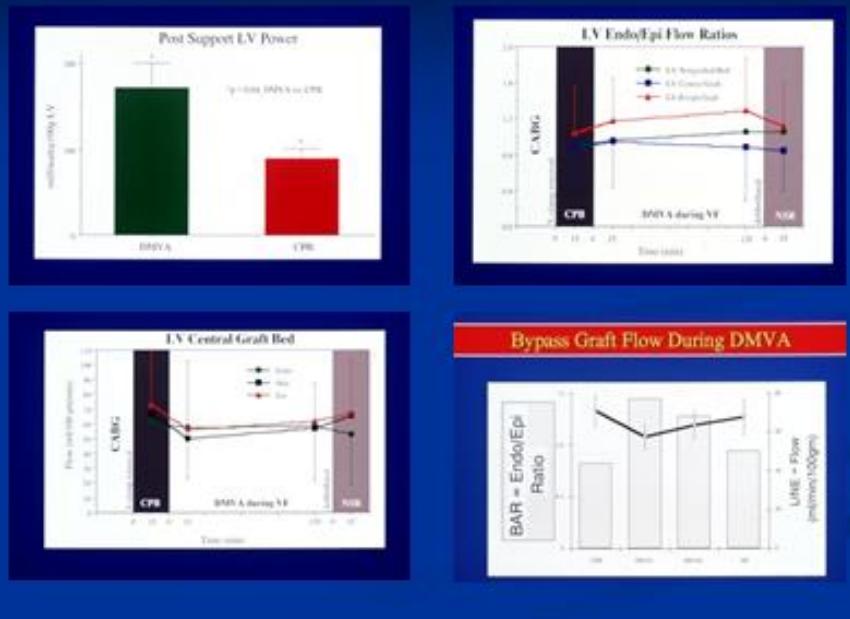
Additional work was done comparing DMVA to support of the heart following surgical revascularization of occluded coronaries using saphenous vein bypass grafts (see preparation below);

## DMVA Following CABG: Experimental Preparation

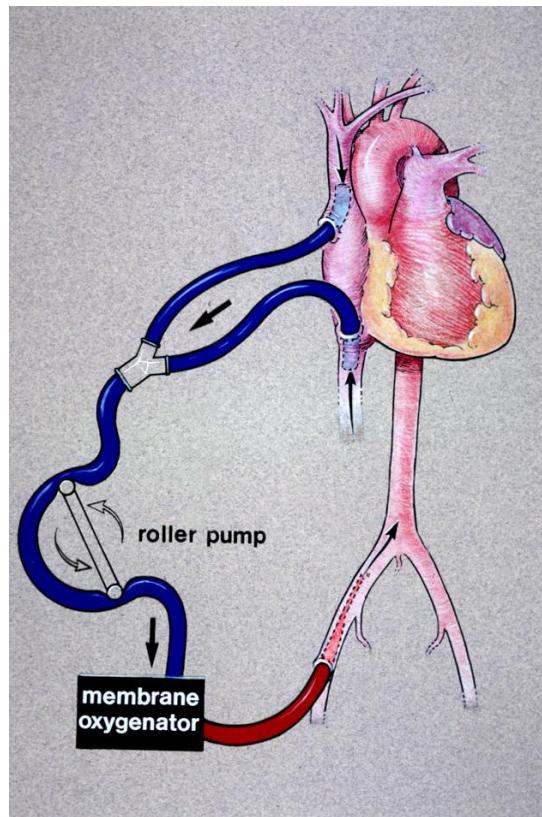


Results demonstrated that DMVA had a favorable effect on perfusion to the revascularized coronary beds with better preservation of myocardial high energy phosphates and improved post-support function (see below):

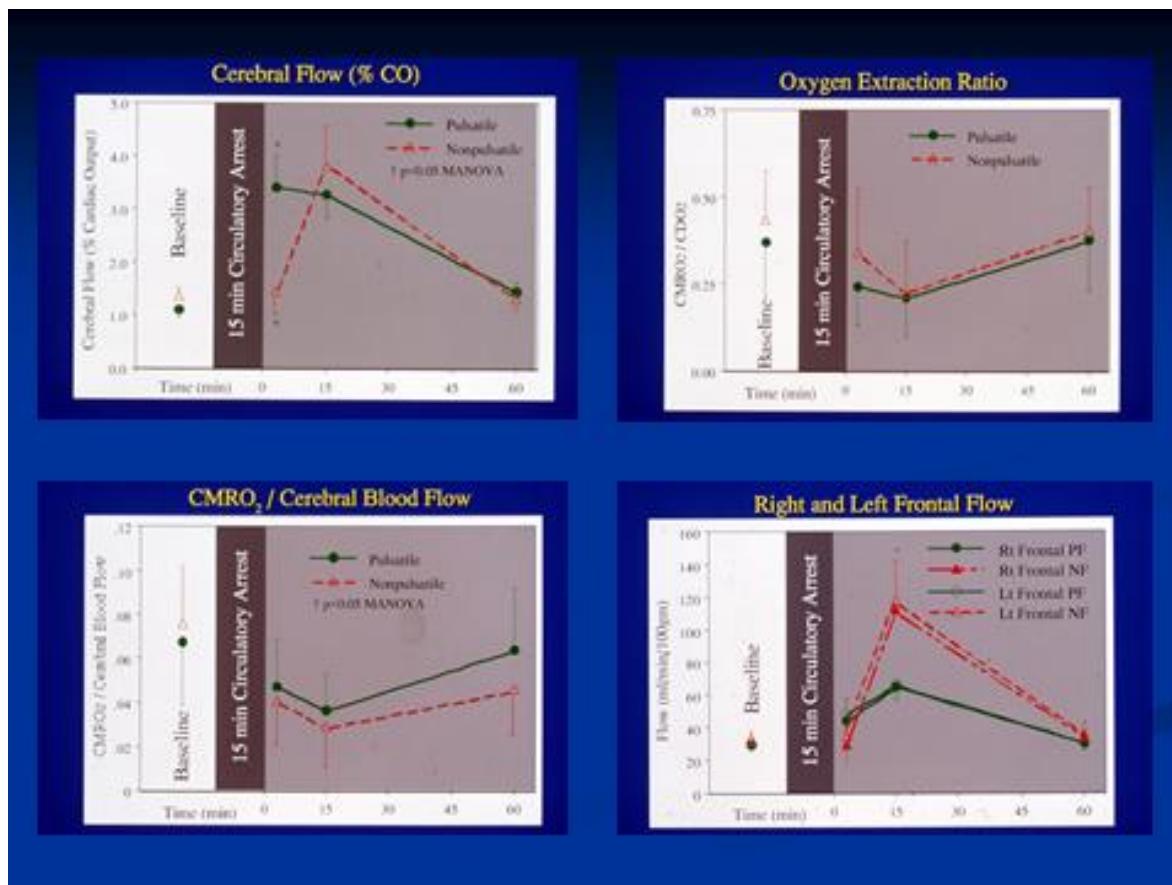
## DMVA VS CPB FOLLOWING CABG



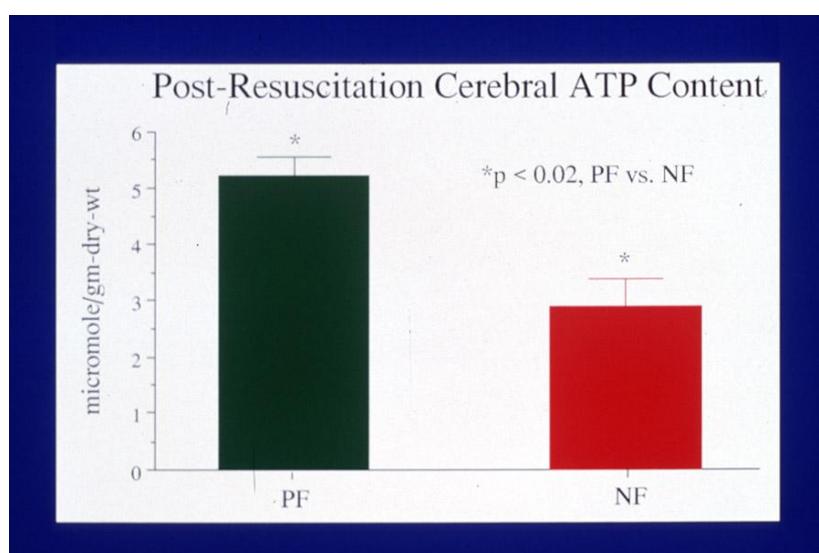
However, the most obvious role for DMVA support remained that of resuscitative circulatory support following cardiac arrest. The only other method that could generate total circulatory support in a relatively reasonable time-frame remains that of modified cardiopulmonary bypass (CPB) units. Therefore, experiments were performed comparing the best possible CPB support to DMVA following cardiac arrest. Below is an illustration of the CPB circuit used in such experiments:



DMVA was compared to CPB following cardiac arrest to determine what differences might exist when both methods were applied after similar periods of arrest. Remember, in the clinical setting DMVA could be applied emergently in 2-3 minutes while it would normally take close 15-30 minutes to employ even partial CPB support. Therefore, these experiments biased results for more favorable CPB. Initial results demonstrated a dramatic difference regarding improved distribution of cerebral flow and resulting cerebral oxygen consumption with DMVA (pulsatile flow) versus CPB (non-pulsatile flow) shown below:



These favorable impacts on cerebral perfusion were the most likely explanation for improved cerebral ATP stores following resuscitation using DMVA (pulsatile flow-PF) versus CPB (nonpulsatile flow). It was felt that the pulsatile nature of resuscitative flow during DMVA support compared to the nonpulsatile flow of CPB might be the most important physiologic difference that could explain these dramatic discrepancies in the experimental results:



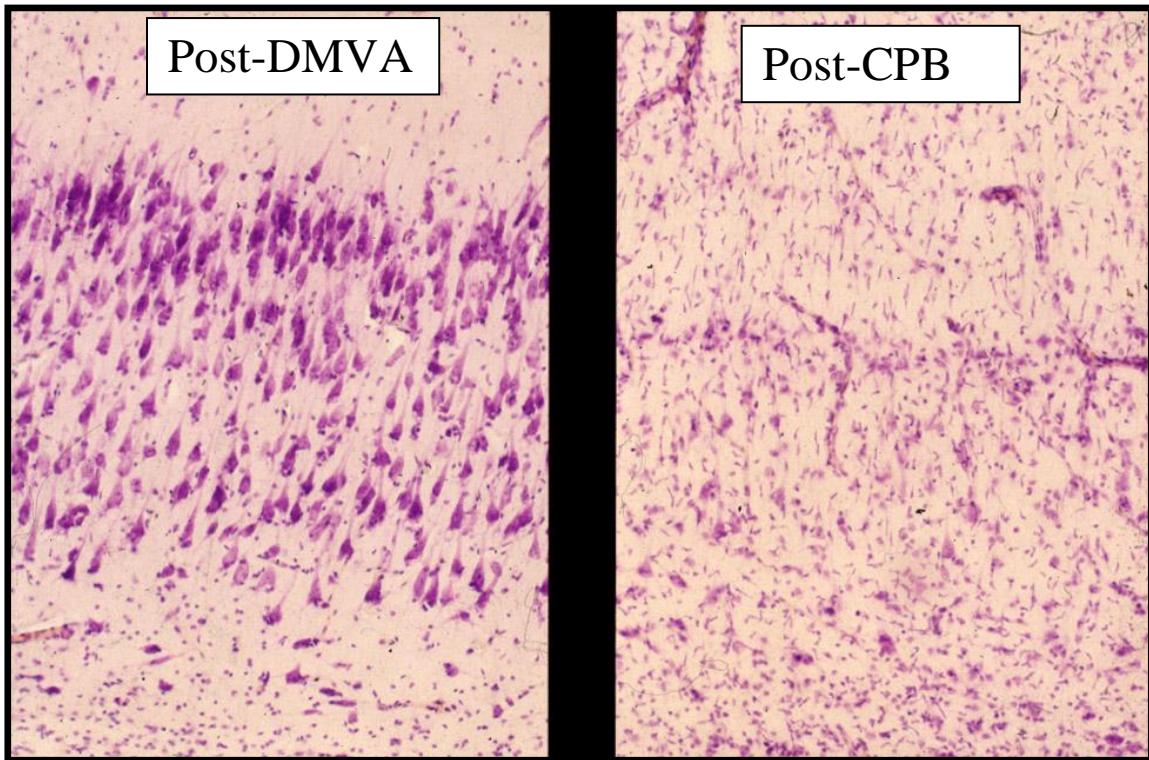
Additional work was then performed in a survival model where canine were resuscitated with DMVA (pulsatile) versus CPB (nonpulsatile) support. The surviving animals had marked improvement with respect to preservation on neurons in the Hippocampus of the brain following DMVA versus CPB as exhibited in the more pronounced purple staining in representative sections from animals following DMVA vs. CPB (see below):



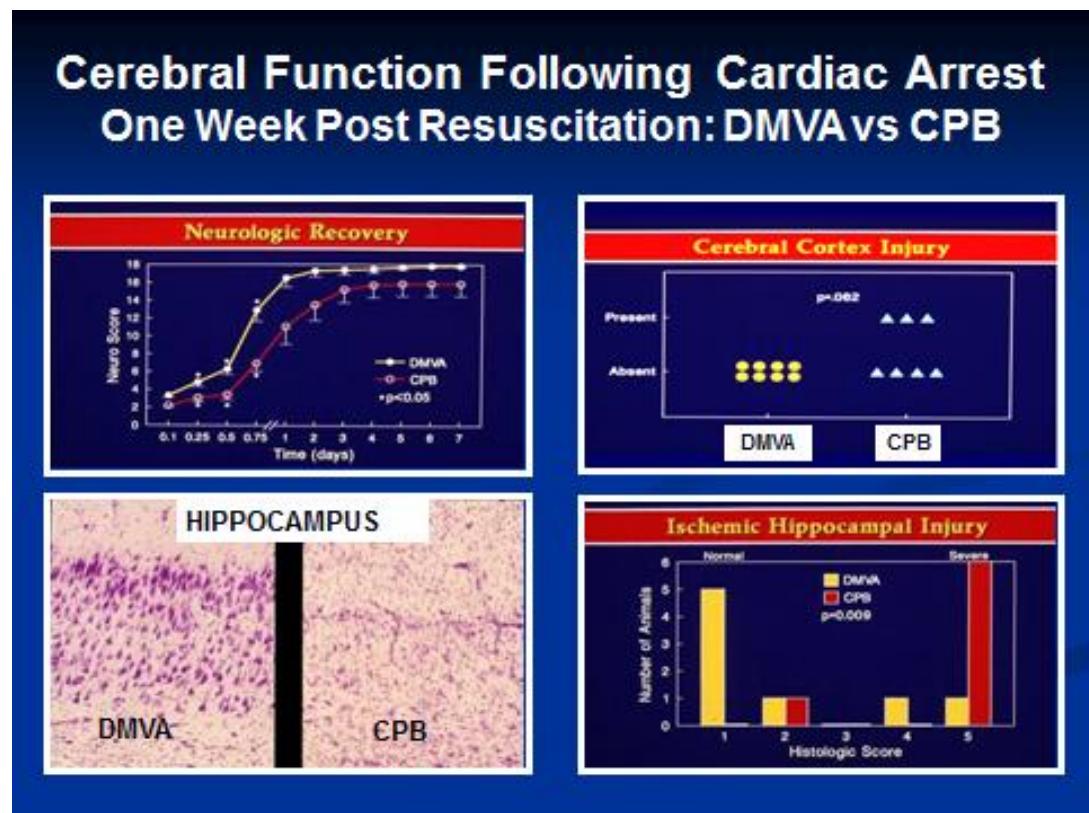
Post-DMVA



Post-CPB



The neurologic recovery and overall hippocampal scores were significantly better in animals following DMVA versus CPB in these survival studies (see below).



Clinical results were also notable using DMVA support. The first patient to receive the device at Duke University Medical Center was successfully bridged to transplantation and remains alive to date more than 10 years later (see abstract below):

## First Successful Bridge to Cardiac Transplantation Using Direct Mechanical Ventricular Actuation

James E. Lowe, MD, Mark P. Anstadt, MD, Peter Van Trigt, MD, Peter K. Smith, MD, Paul J. Hendry, MD, Mark D. Plunkett, MD, and George L. Anstadt, VMD

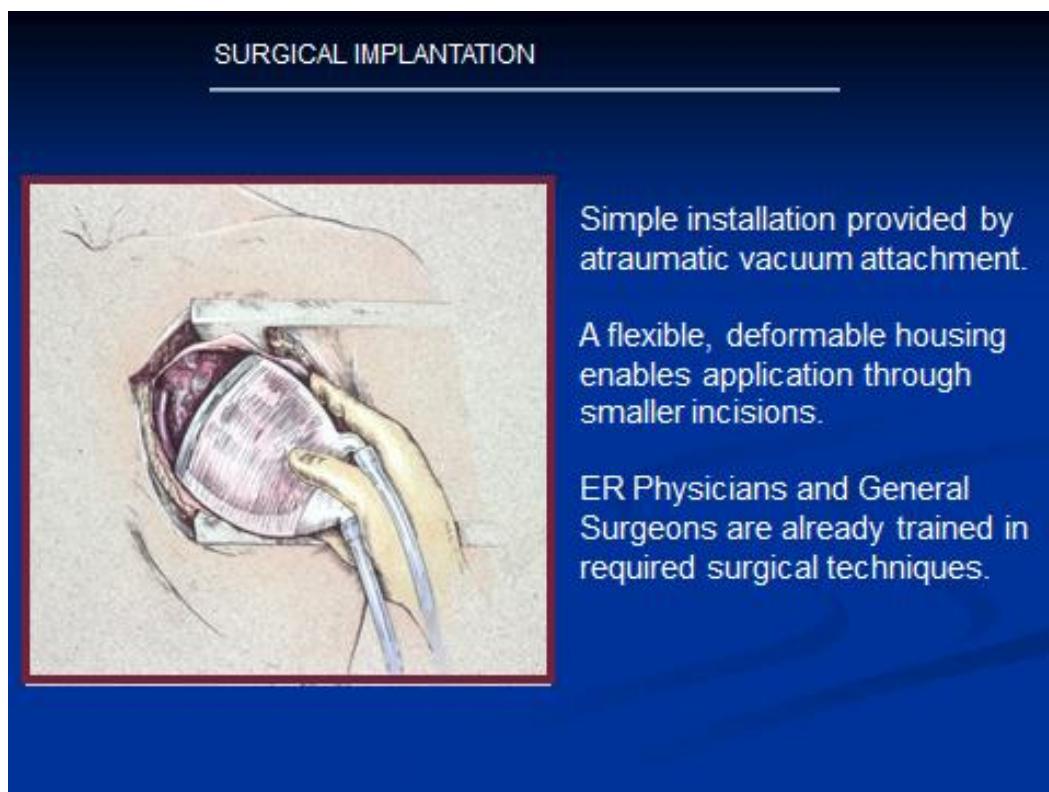
Department of Surgery, Duke University Medical Center, Durham, North Carolina

Currently available ventricular assist devices are technically difficult to implant, require continuous anticoagulation, and are associated with hemorrhagic and thromboembolic complications. Direct mechanical ventricular actuation is a biventricular assist device that can be applied in 3 to 5 minutes through a left anterior thoracotomy and has no direct blood contact or need for anticoagulation. The present study was designed to determine the effects of direct mechanical ventricular actuation in total biventricular circulatory support. Cardiogenic shock refractory to standard therapy developed in 2 patients awaiting cardiac transplantation. Direct mechanical ventricular actuation was applied and provided immediate hemodynamic stabilization in both. All inotropic agents and intraaortic balloon support were then discontinued. Fifty-six hours of circulatory support bridged the first patient to successful cardiac transplan-

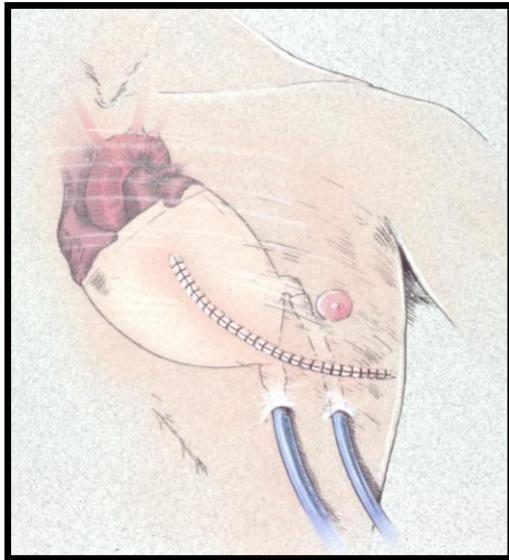
tation without complication. The patient is alive and well more than 1 year later without incident of infection or rejection. The second patient suffered cardiac arrest and required closed chest cardiopulmonary resuscitation before device application. After 45 hours of support, it was determined that irreversible neurologic injury had occurred and direct mechanical ventricular actuation was discontinued. Neither patient's native heart exhibited any histologic evidence of device-related trauma. Direct mechanical ventricular actuation has undergone limited clinical investigation since its original description 25 years ago, but in these initial trials, the device has proved effective. The concept of mechanically actuating the ventricles appears to be a valuable, yet under-utilized method of total circulatory support.

(Ann Thorac Surg 1991;52:1237-45)

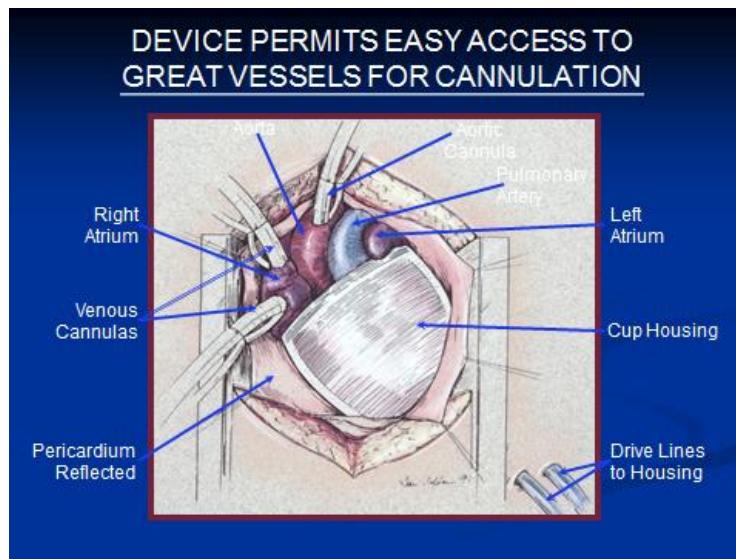
The device can be applied rapidly (2-3 minutes) thru an anterior thoracotomy (see below):



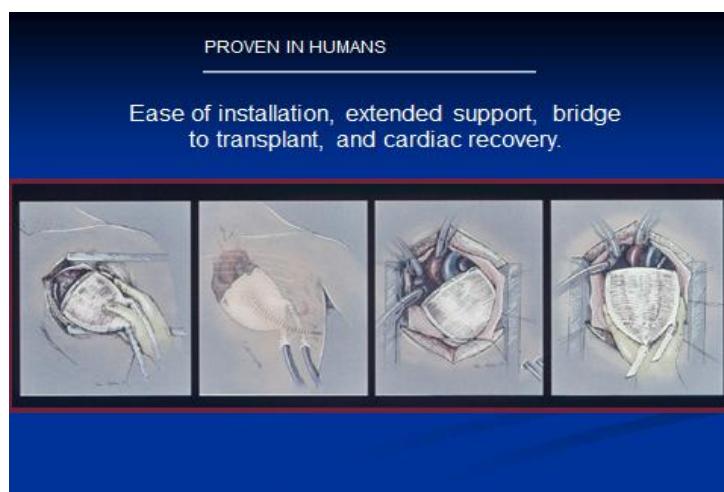
Once applied the chest can be closed for transport of the patient (see below):



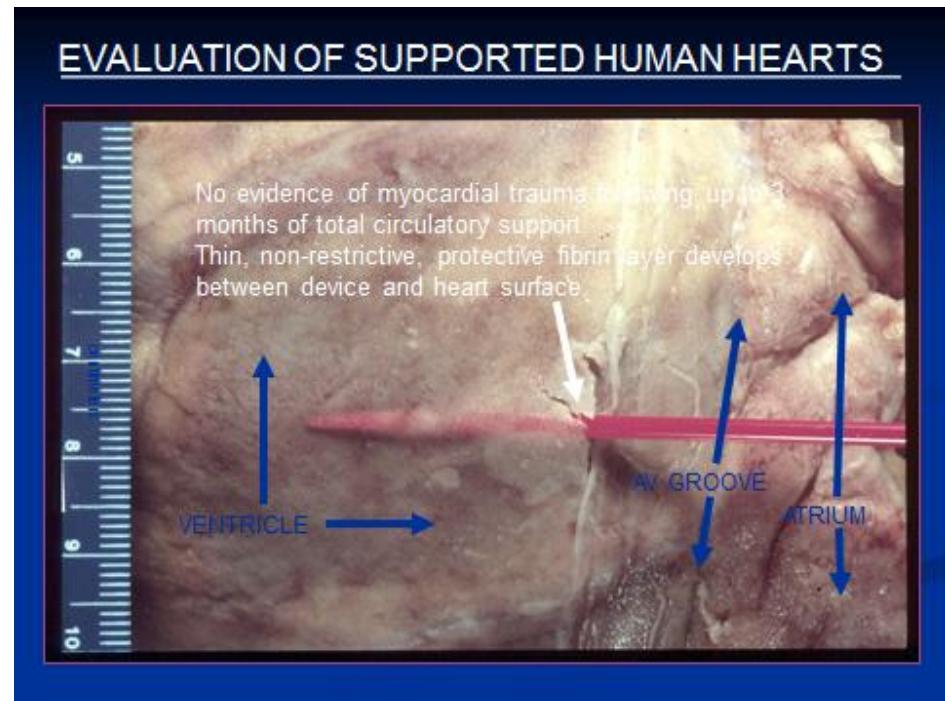
Other methods of long-term circulatory support can then be instituted by transitioning to CPB as a needed step in such considerations (see below):



This can be summarized as shown below:



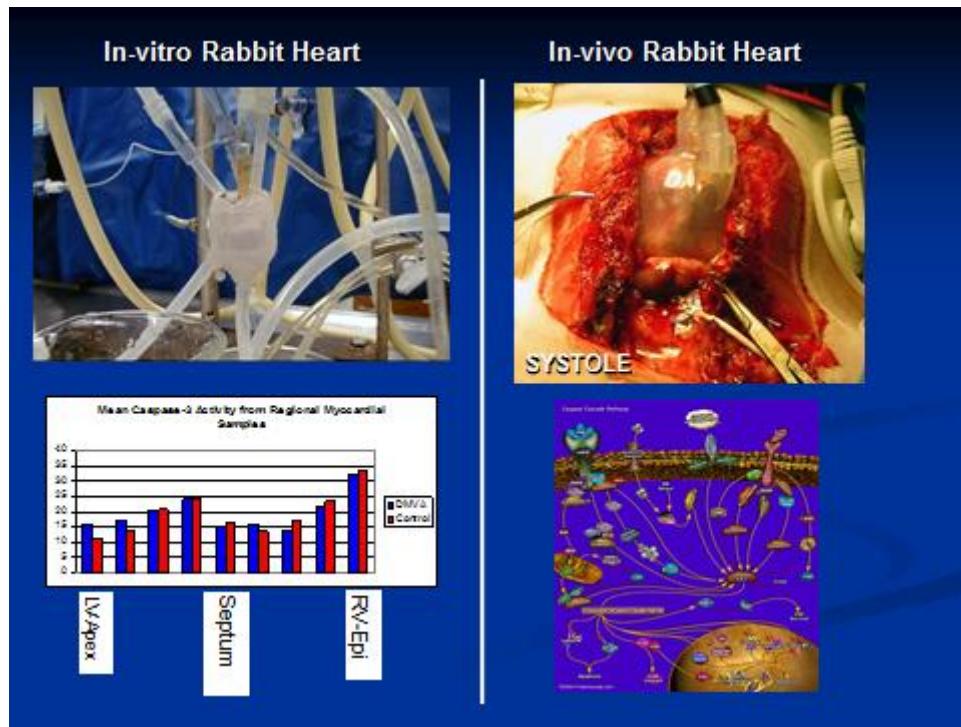
Pathologic evaluation in patients supported by DMVA has shown no evidence of myocardial damage even after up to 3 months of support (see below):



Research following these clinical findings began focusing on support of the failing heart using smaller animal models. The DMVA cup technology was reduced to smaller sizes using the same designs as proven in animal studies (see below):



The rabbit model was the smallest animal model used for experimental DMVA support and was comparable to the human neonate with respect to head size (see below):



Using the rabbit model it was demonstrated that DMVA could support the failing heart with favorable effects on the myocardium with respect to cell signaling indicating a favorable impact on myocardial recovery (see results below):

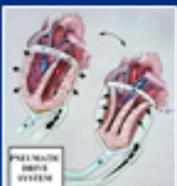
**WRIGHT STATE UNIVERSITY**

# Direct Mechanical Ventricular Actuation of the Acutely Failing Heart Attenuates Maladaptive Cell Signaling

MP Anstadt, SA Kerna, CJ Wozniak, BA Schmitt, RJ Darner, S Budharaju, and LJ Prochaska  
 Department of Surgery & Biomedical Sciences, Boonshoft School of Medicine Wright State University Dayton, OH

## Introduction

Cardiogenic shock (CVS) is associated with low cardiac output and can be treated with blood pumps or ventricular assist devices (VADs). Mechanism of "relaxation" by VADs during acute severe heart failure (ASHF) can improve myocardial recovery. However, VADs result in systemic  $\Delta$  compliance increases which generate the maladaptive cell signaling of heart failure. Thus, mechanical ventricular actuation (MVA) is a novel and exciting assist device that can be rapidly applied for supporting both systemic and diastolic ventricular pump function.



**PULMONARY VEIN SYSTEM**

## Materials & Methods

New Zealand white rabbits (n=42) underwent sternotomy and were anesthetized for hemodynamic monitoring. Control (i.e. sham-ventilated) and MVA-ventilated hearts were pressurized. Animals received either DMDA or no additional support (N). At 20, 40, or 120 min of DMDA treatment (DMDA<sub>20</sub>, DMDA<sub>40</sub>, DMDA<sub>120</sub>), hearts were removed and then rapidly frozen. Immunoblotting and densitometry was performed on CV and RV cell lysates. Immunoblotting and protein quantification of rabbit heart myosin, Gα<sub>i</sub> (Gα<sub>i</sub>), heart muscle protein 70 (HSP70), myosin-2, myosin-7, or cytoskeletal 2 (glutathione S-transferase, GSTM2), Gα<sub>i</sub> activity, myosin binding protein kinase, and myosin-2 activity (assay at 400 nm for the 10 minutes, read at 450 nm) of protein fractions. Immunoblotting/densitometry was measured by densitometry and expressed as fold change using densitometry at 20 min. Statistical analysis: Results are presented as mean  $\pm$  SEM and compared between groups using a one-way ANOVA and a post-hoc Least Squared Differences (LSD) pairwise t-test (Statistica 8.0).

## Discussion

The DMDA model requires mechanical ventricular activity, which can be induced by uncoupling of endogenous stroke at about 100 Hz. The resulting increase in activated HSP70 & Gα<sub>i</sub> and endogenous protein kinase activity in response to successive CV cell lysates. This led to maladaptive cell signaling mediated by protein kinase activation. DMDA attenuated the observed maladaptive cellular response. These results are best explained by reductions in myocardial cell stress during DMDA support. Further analysis of maladapted protein kinase may aid in defining the maladaptive mechanisms pertaining to heart failure.

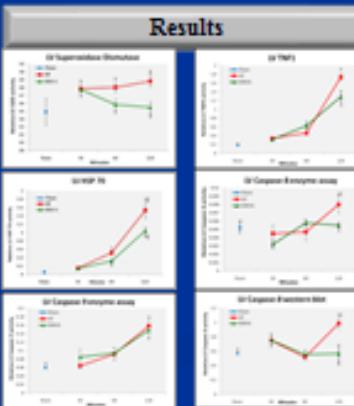


**DMDA Model**

## Purpose

Prior studies have demonstrated DMDA attenuates maladaptive signaling (ASD) activity in the acutely failing heart.<sup>1</sup> This has favorable implications regarding DMDA's effects on heart failure, stroke, degradation, and subsequent myocardial remodeling. These findings are likely related to reduced myocardial stress during DMDA suggested by Daigle, Jarrar, O'Dowd.

## Results



## Conclusion

Cardiogenic shock is associated with a high mortality unless the underlying cause can be effectively treated in a timely fashion. Diagnosing ventricular dysfunction remains a myocardial challenge, while treatments in maladaptive cell signaling. DMDA can effectively treat cardiogenic shock by rapidly reducing pump function without the complications of blood vessels.

The results of this study demonstrated that DMDA supports stress protein kinase cell signaling in the acutely failing heart. The findings corroborate recent investigations which demonstrated DMDA's favorable effects on myocardial stress.<sup>1</sup> The current study provides additional compelling evidence that DMDA, despite the acutely failing heart, may reduce tendencies for subsequent myocardial remodeling.

**ACKNOWLEDGEMENTS**

1. Anstadt MP, Prochaska LJ, Kerna SA, et al. Attenuation of Maladaptive Cell Signaling in Acutely Failing Rabbit Hearts by Mechanical Ventricular Actuation. *Am J Physiol Heart Circ Physiol* 2010; 299: H105-H114.

2. Anstadt MP, Prochaska LJ, Kerna SA, et al. Mechanical Ventricular Actuation Attenuates Maladaptive Cell Signaling in Acutely Failing Rabbit Hearts. *Am J Physiol Heart Circ Physiol* 2010; 299: H105-H114.

3. Anstadt MP, Budharaju S, Kerna SA, et al. Mechanical Ventricular Actuation Attenuates Maladaptive Cell Signaling in Acutely Failing Rabbit Hearts. *Am J Physiol Heart Circ Physiol* 2010; 299: H105-H114.

4. Anstadt MP, Prochaska LJ, Kerna SA, et al. Mechanical Ventricular Actuation Attenuates Maladaptive Cell Signaling in Acutely Failing Rabbit Hearts. *Am J Physiol Heart Circ Physiol* 2010; 299: H105-H114.

**REFERENCES**

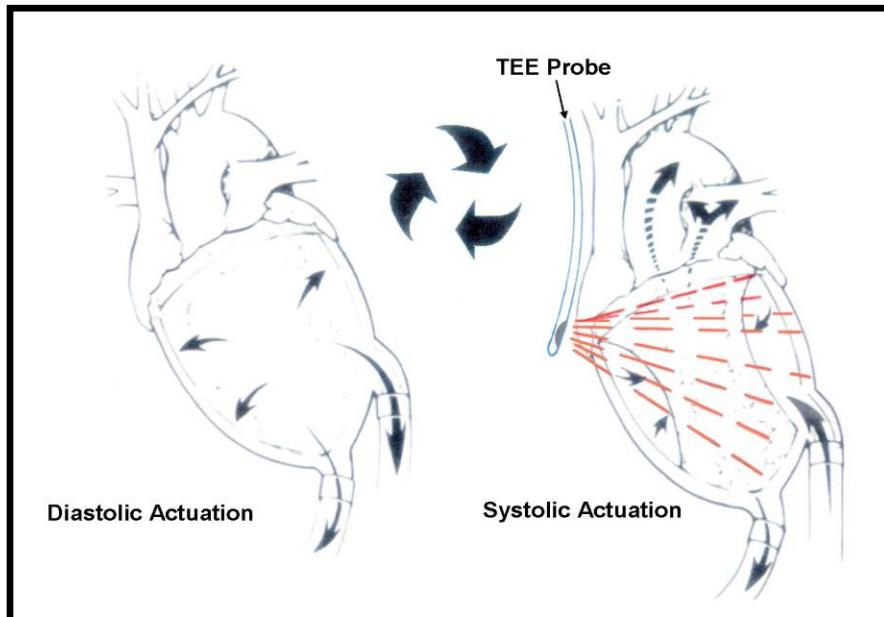
1. Anstadt MP, Prochaska LJ, Kerna SA, et al. Attenuation of Maladaptive Cell Signaling in Acutely Failing Rabbit Hearts by Mechanical Ventricular Actuation. *Am J Physiol Heart Circ Physiol* 2010; 299: H105-H114.

2. Anstadt MP, Prochaska LJ, Kerna SA, et al. Mechanical Ventricular Actuation Attenuates Maladaptive Cell Signaling in Acutely Failing Rabbit Hearts. *Am J Physiol Heart Circ Physiol* 2010; 299: H105-H114.

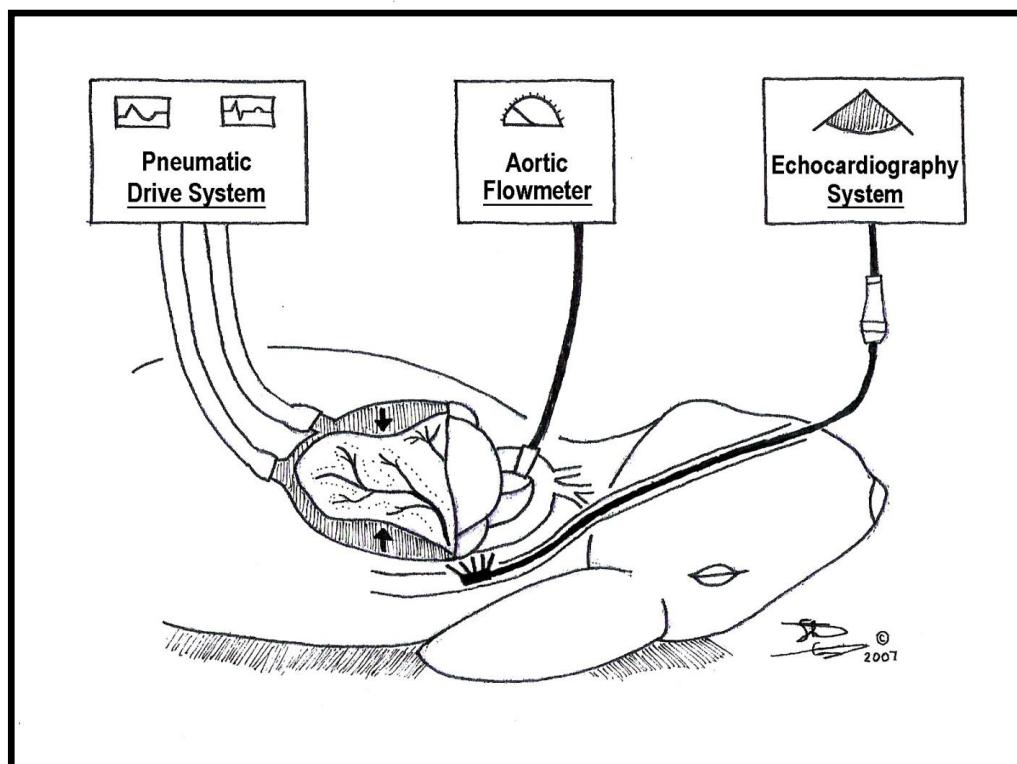
3. Anstadt MP, Budharaju S, Kerna SA, et al. Mechanical Ventricular Actuation Attenuates Maladaptive Cell Signaling in Acutely Failing Rabbit Hearts. *Am J Physiol Heart Circ Physiol* 2010; 299: H105-H114.

4. Anstadt MP, Prochaska LJ, Kerna SA, et al. Mechanical Ventricular Actuation Attenuates Maladaptive Cell Signaling in Acutely Failing Rabbit Hearts. *Am J Physiol Heart Circ Physiol* 2010; 299: H105-H114.

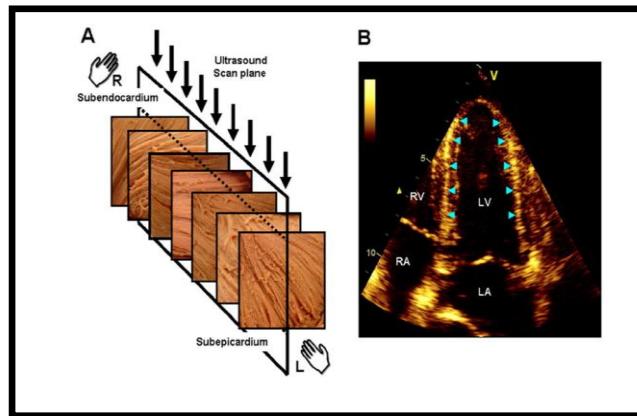
With the addition of echocardiographic, the functional aspects of how DMVA can effect myocardial contraction were enabled. Transesophageal (TEE) and trans-venous ECHO imaging provided the windows for such interrogation (see below):



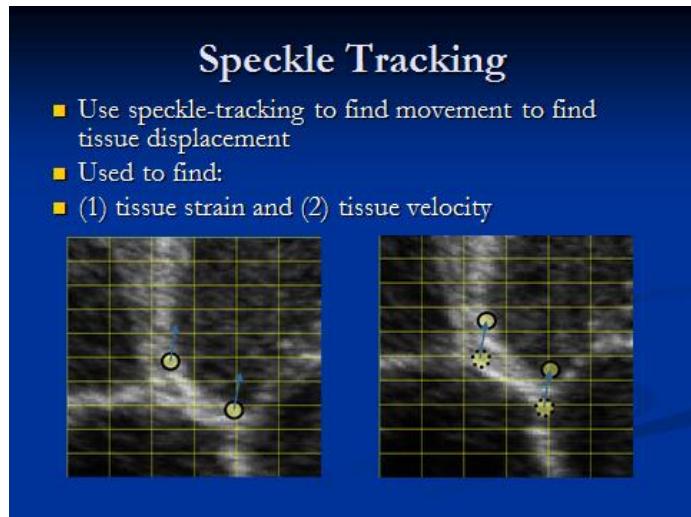
With ECHO analysis the complex manner in which myocardial contraction occurs can be characterized both graphically and with objective numeric analysis. The rabbit model was the first utilized to interrogate DMVA support of the failing heart (see below):



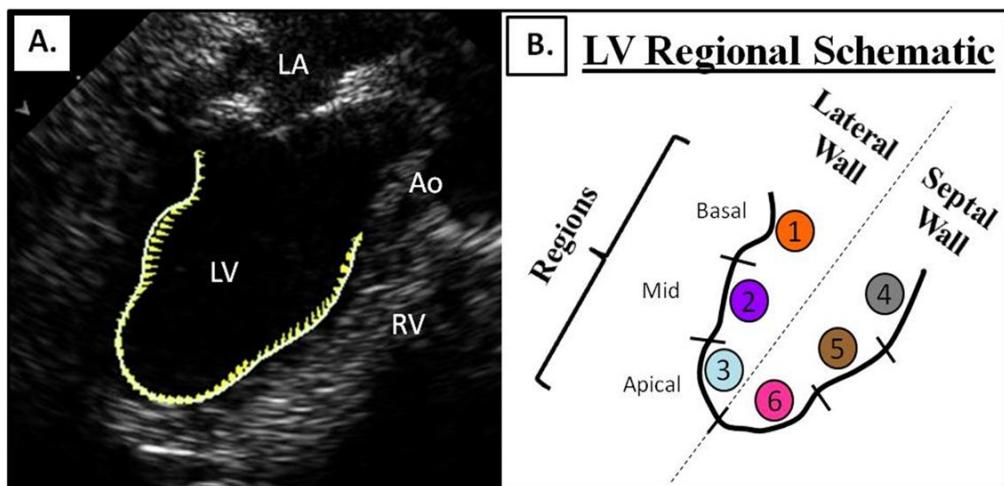
Speckle tracking using proprietary ECHO software enabled myocardial strain to be assessed in the heart before, during and after DMV support. Figure below illustrates how ultrasound imaging can visualize the myocardium to obtain strain imaging.



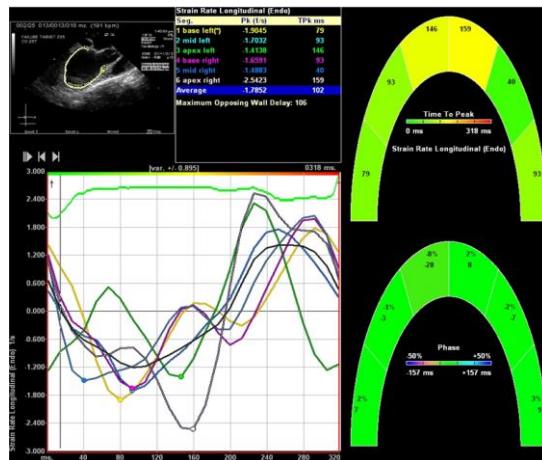
Once ECHO imaging is acquired, the technique of speckle tracking is utilized to calculate regional and global myocardial strain as depicted in the below diagram:



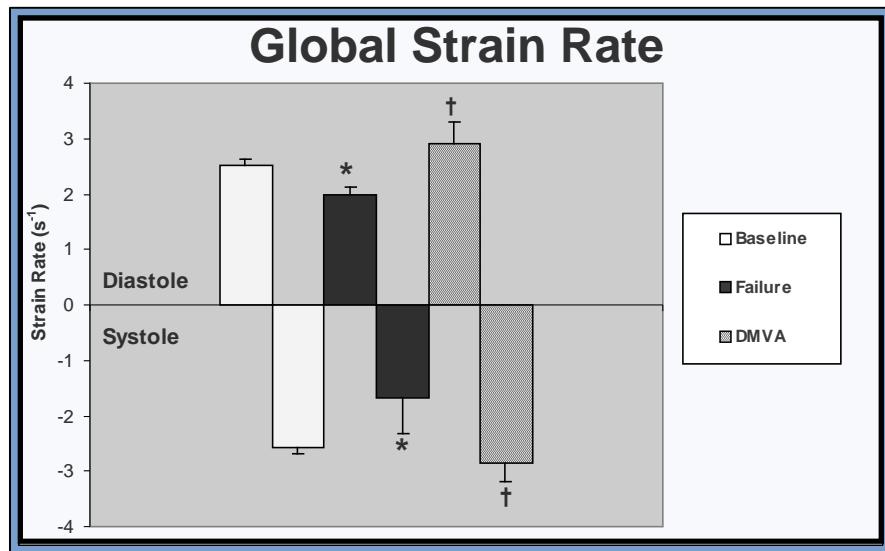
For studies carried out by our laboratory, the long axis of the left ventricle was interrogated using speckle tracking proprietary software. The left ventricle was divided into 6 regions to do analysis on both regional and global myocardial function as depicted below:



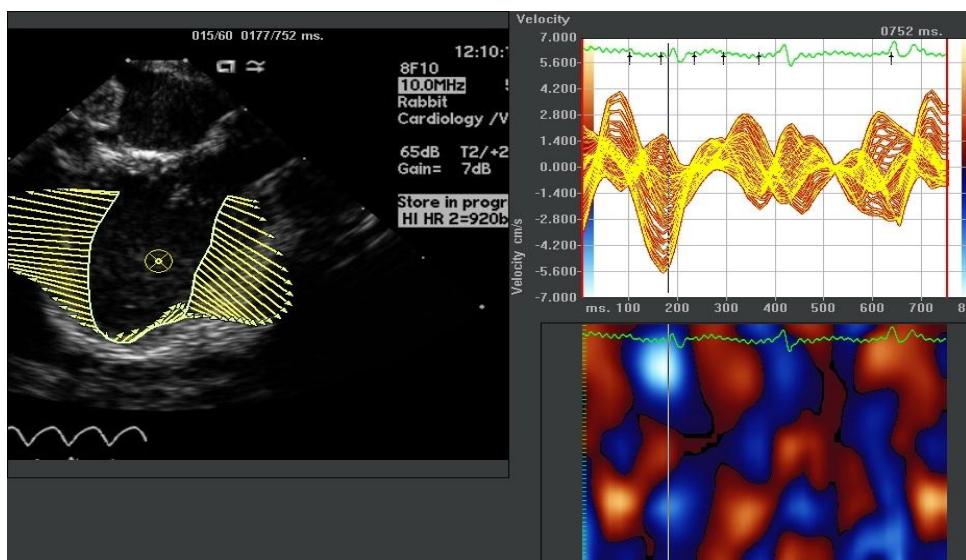
A snapshot of a representative ECHO strain image is shown below:



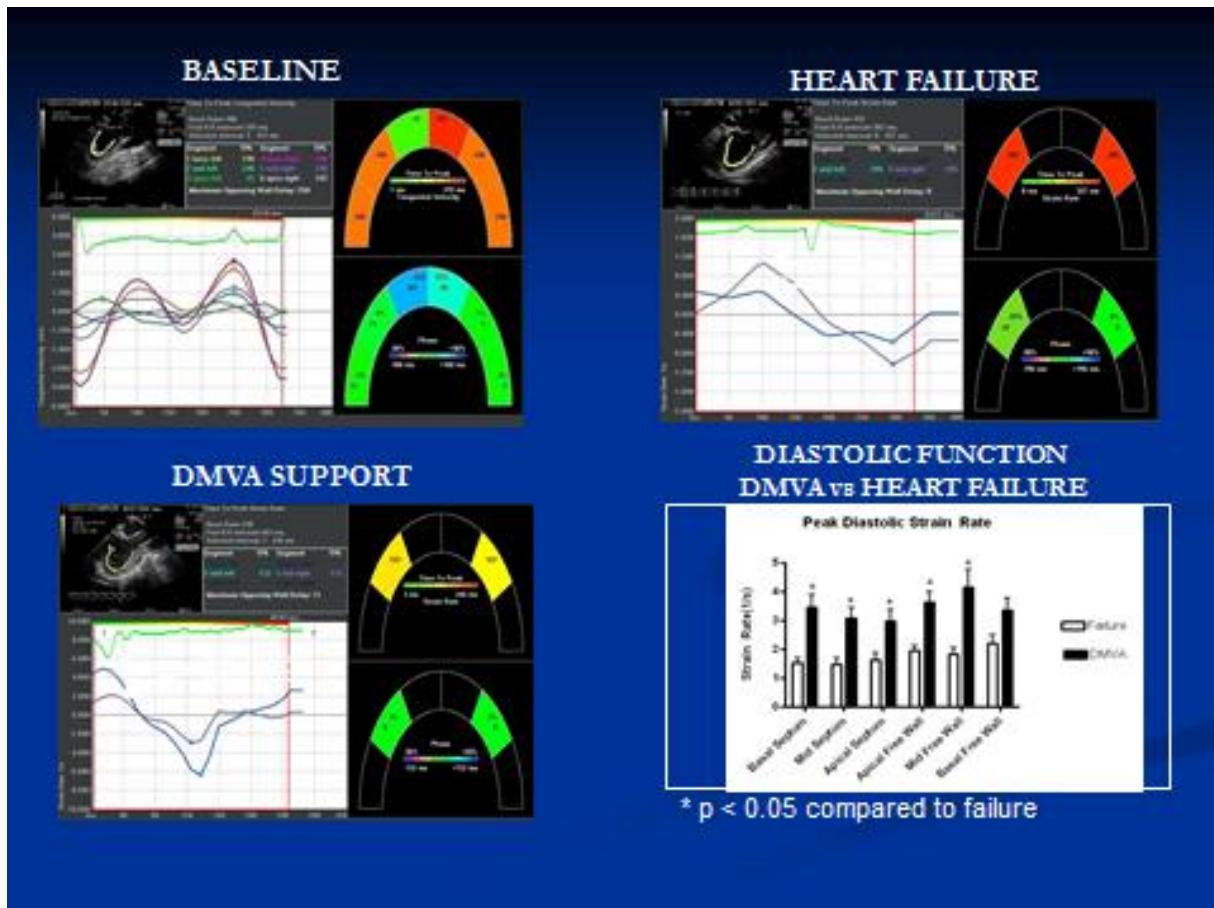
The data below compares global functions expressed as myocardial stain in rabbits during baseline, failure and subsequent DMVA support. Note DMVA returned both systolic and diastolic function to values greater than control.



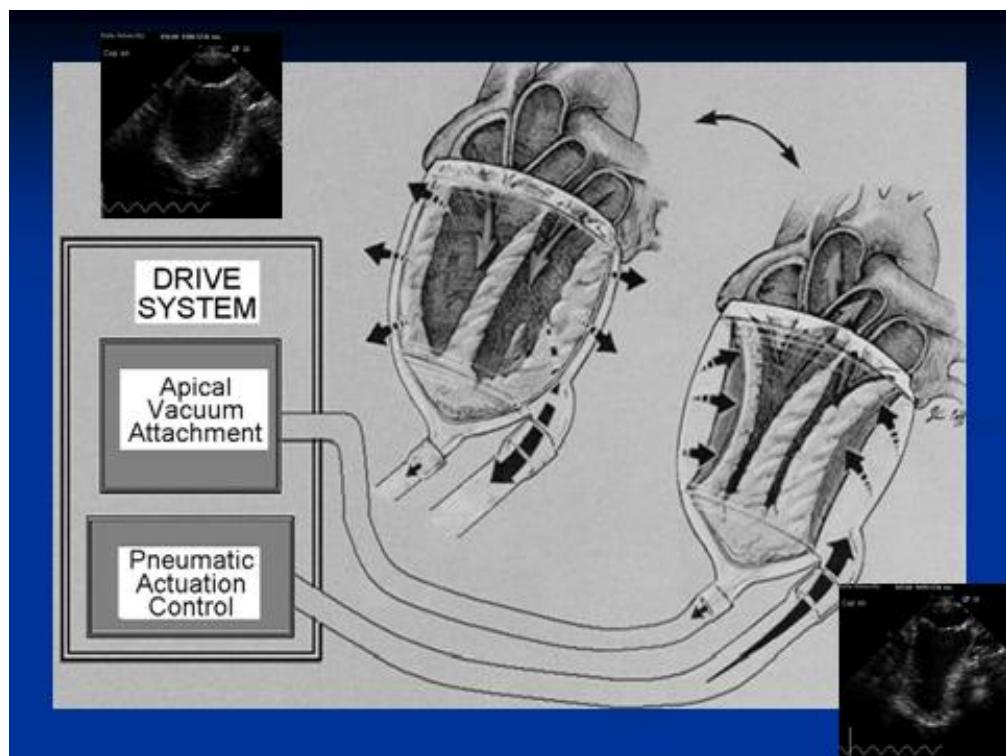
The augmentation of diastolic function, as depicted in the outward arrows of the snapshot below represent the unique capability of DMVA support compared to other DCC devices as explained earlier, see figure below:



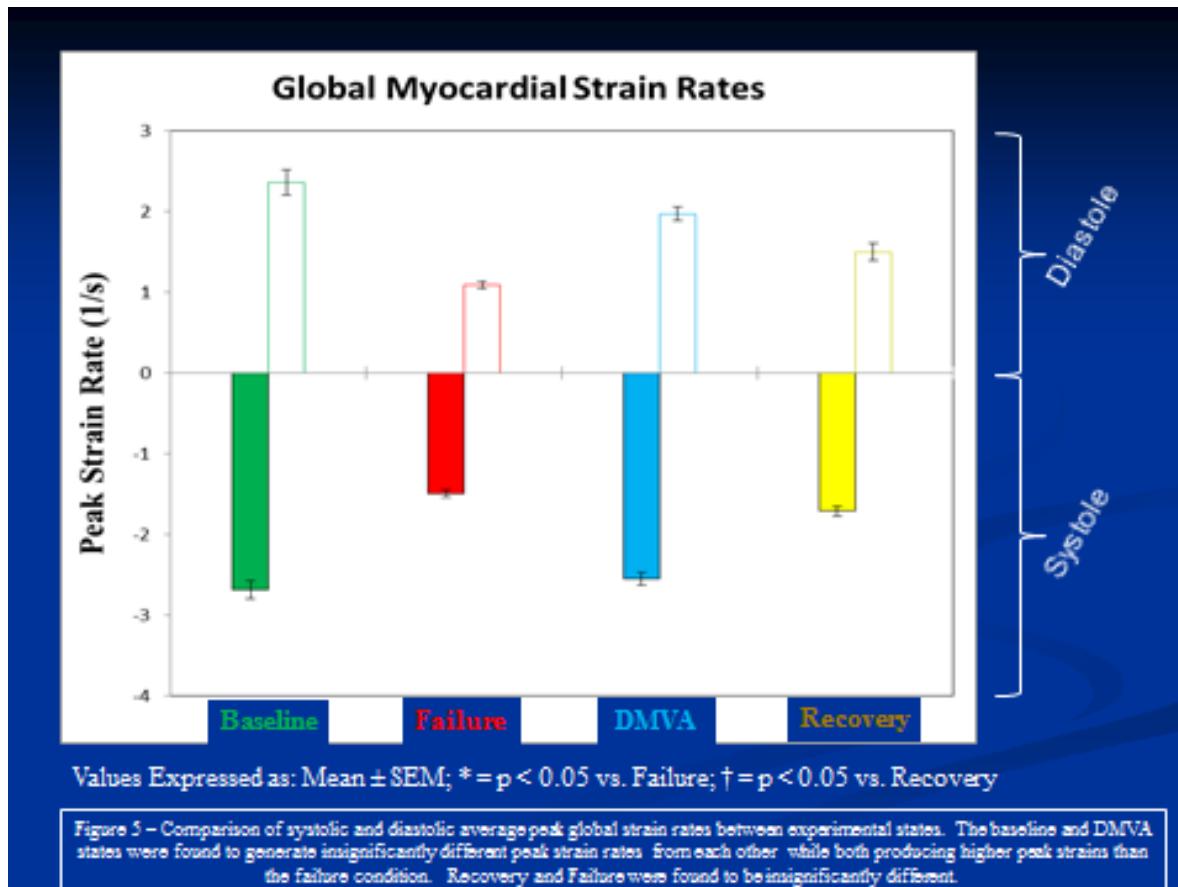
The ability of DMVA to provide diastolic augmentation to the failing and arrested heart has now been demonstrated and published as shown below:



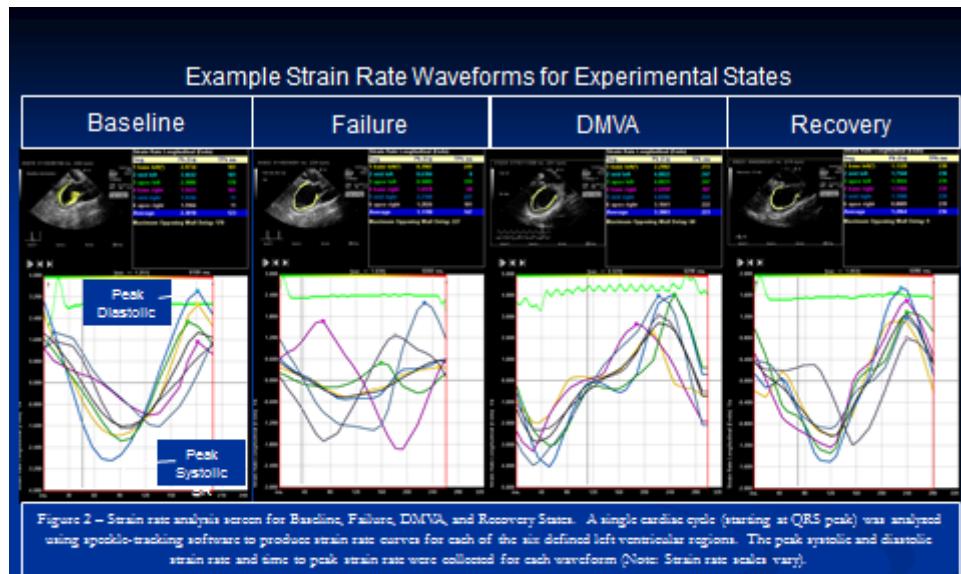
The use of ECHO to interrogate the heart during support with DMVA has been a primary means of analysis of DMVA drive functionality in the present project, (see below):



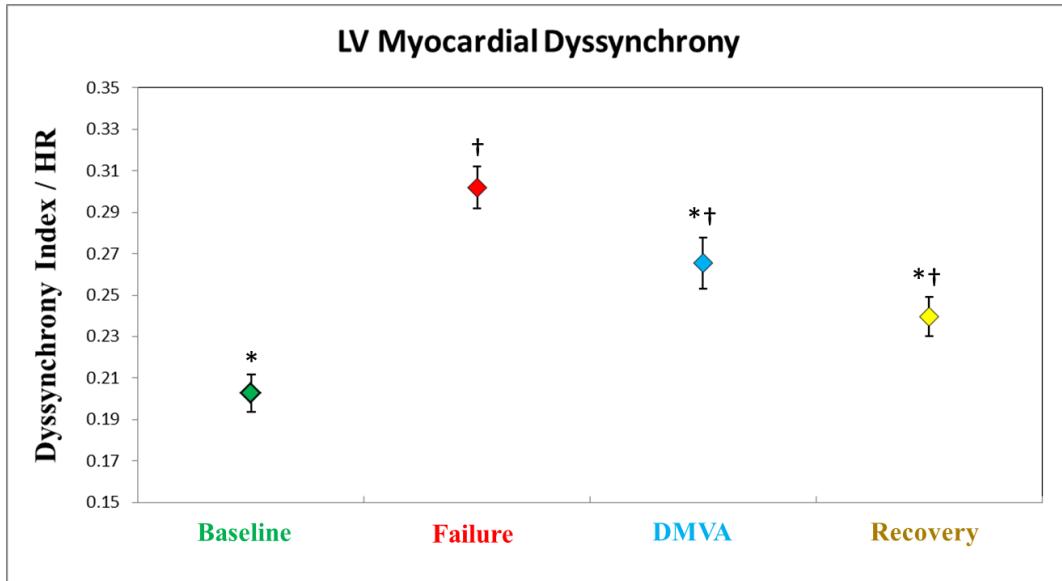
ECHO stain analysis has also demonstrated how DMVA not only improves myocardial function of the failing heart but also returns mechanical synchrony to a more normal state:



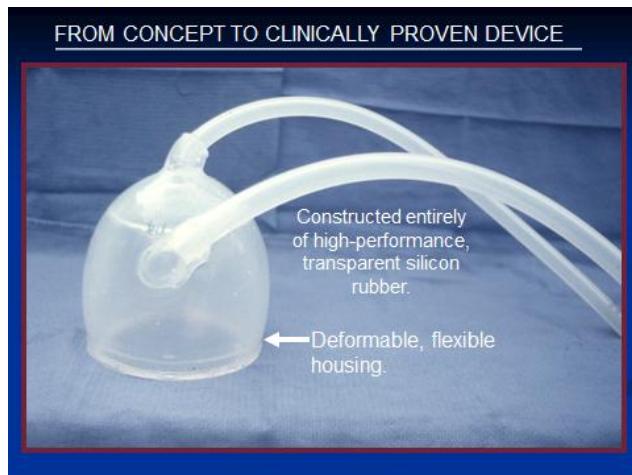
The snapshots below demonstrate graphically how DMVA returning synchrony during failure:



The return of synchrony can be numerically depicted as shown below:



These methods of analysis along with proven cup design (shown below) were utilized in this project:



## 5. CONCLUSION

This project successfully accomplished its intended goal of developing a device for rapid, effective, circulatory support for remote areas. The importance of this accomplishment is that DMVA can be made available to re-establish normal hemodynamics in patients suffering circulatory arrest in the field. The portable, compact, user-friendly DMVA drive system can be operated with minimal expertise. The AD can be utilized as a life-saving device by Military Medical Personnel in the field. A circulatory support for such application is otherwise not available to save soldiers or civilians outside the hospital environment. Reducing DMVA's operation to a user friendly, AD makes it more feasible for use in the hospital setting as well. Future goals will be to utilize the new prototype design in clinical trials to demonstrate efficacy for resuscitative circulatory support.

## 6. PUBLICATIONS, ABSTRACTS, and PRESENTATIONS

### SCIENTIFIC PUBLICATIONS:

**Anstadt MP**, Budharaju S, Darner RJ, Schmitt BA, Prochaska LJ, Pothoulakis AJ, Portner PM. *Ventricular Actuation Improves Systolic and Diastolic Myocardial Function in the Small Failing Heart*, Annals Thorac Surg 2009;88:1982-8.

McConnell PI, **Anstadt MP**, del Rio CL, Preston T, Ueyama Y, Youngblood B. *Cardiac Function after Acute Support with Direct Mechanical Ventricular Actuation in Chronic Heart Failure*. In PRESS: ASAIO 2014.

### ABSTRACTS/PRESENTATIONS:

Budharaju S, Pothoulakis AJ, Kerns SA, Schmitt B, Darner RJ, Prochaska LJ, Portner PM, **Anstadt MP**. *Direct Mechanical Ventricular Actuation Significantly Augments Left Ventricular Function In Failing Rabbit Heart Model*. Circ, 2008;118(18), suppl 2,12.

**Anstadt MP**, Kerns S, Wozniak CJ, Schmitt BA, Darner RJ, Budharaju S, Prochaska LJ. *Direct Mechanical Ventricular Actuation of the Acutely Failing Heart Attenuates Maladaptive Cell Signaling*. Circulation 2009;120:S1490.

Schmitt BA, Reynolds DB, Troche K, Gallimore JJ, Gargac SM, Darner RJ, and **Anstadt MP**. *Defining Power Specifications for Pediatric Direct Mechanical Ventricular Actuation Systems*. In: 2009 Biomedical Engineering Society Annual Meeting: October 7-10, 2009; Pittsburgh , PA.

Swartzmiller KM, Schmitt BA, Reynolds DB, Perez-Tamayo RA, Darner RJ, **Anstadt MP**. *A Simple Mock Circulatory System for Testing Direct Mechanical Ventricular Actuation*. In: 2010, Biomedical Engineering Society Annual Meeting, Oct 6-9, 2010; Austin, TX.

McConnell PI, Del Rio C, Preston T, Schmidt BA, Darner RJ, **Anstadt MP**. *Short-Term Support via Direct Mechanical Ventricular Actuation Improves Cardiac Function in Chronically Failing Hearts*. Accepted for presentation at Annual Meeting of the International Heart and Lung Society: 11/19/2010.

Swartzmiller KM, Schmitt BA, Reynolds DB, Perez-Tamayo RA, Darner RJ, **Anstadt, MP**. *A Simple Mock Circulatory System For Testing DMVA*. Presented at the 57<sup>th</sup> Annual Conference, ASAIO 2011:57(2) 115.

Schmitt BA, Swartzmiller KM, Reynolds DB, Darner RJ, Perez-Tamayo RA, **Anstadt MP**. *Pneumatic Drive Requirements for Direct Mechanical Ventricular Actuation*. Presented at the 57<sup>th</sup> Annual Conference, ASAIO 2011:57(2) 115.

McConnell PI, Del Rio C, Preston T, Schmidt BA, Darner RJ, **Anstadt MP**. *Short-Term Support Via Direct Mechanical Ventricular Actuation Improves Cardiac Function in Chronically Failing Hearts*. Journal of Heart and Lung Transplantation. April 2011:S49-S49.

Schmidt BA, Garvin NJ, Budharaju S, Reynolds DB, Darner RJ, Prochaska LJ, **Anstadt MP**. *Direct Ventricular Compression Improves Mechanical Synchrony of the Acutely Failing Heart*. Circulation. 2012. 126:A326.

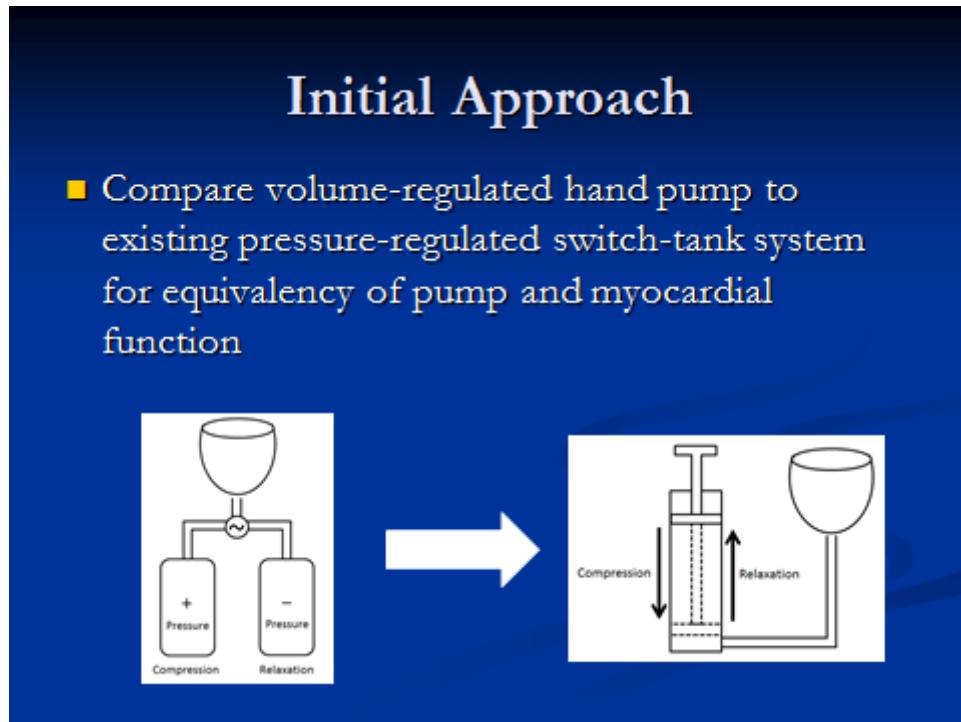
Metzger SA, Schmitt BA, Carnahan KT, Carver DE, Reynolds DB, **Anstadt MP**. *Novel Use of Ultrasound to Characterize Strain Rates in Mock Heart Ventricles*. Accepted for presentation at the 2013 Biomedical Engineering Society Annual Meeting, Seattle, Washington, September 25-28, 2013.

## 7. INVENTIONS, PATENTS, and LICENSES

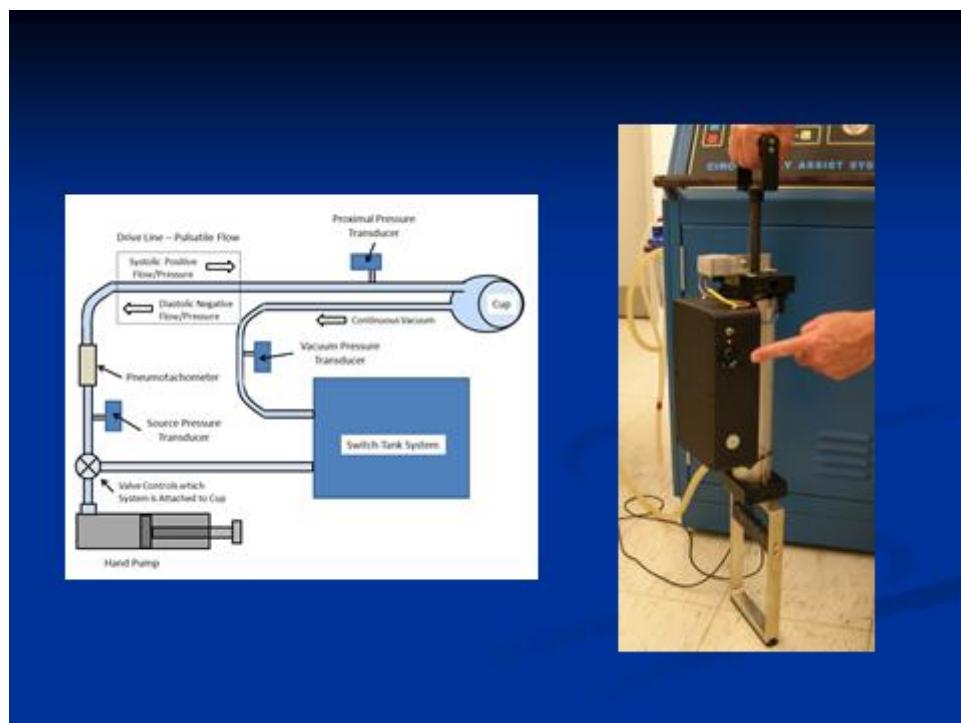
Nothing to report

## 8. REPORTABLE OUTCOMES

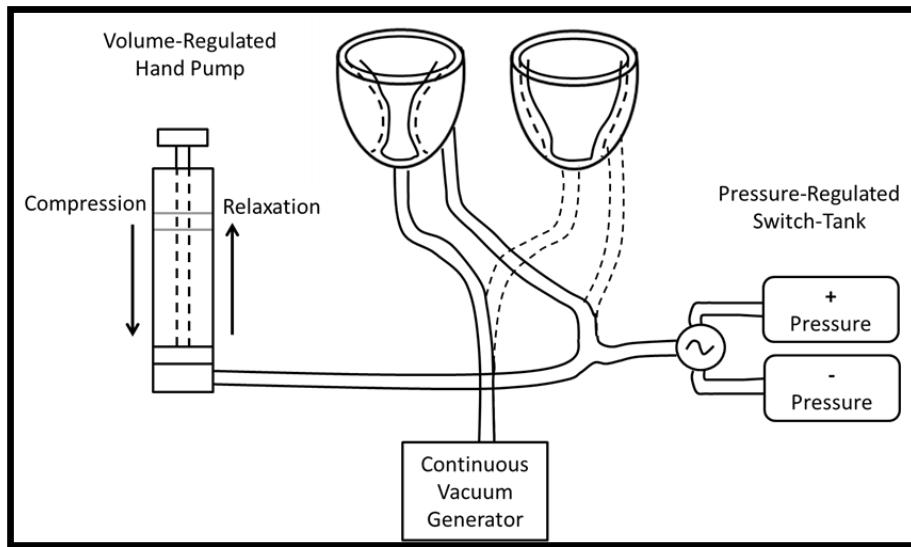
Given the understanding that a HP could achieve similar functionality as the ST drives, the project followed the below approach:



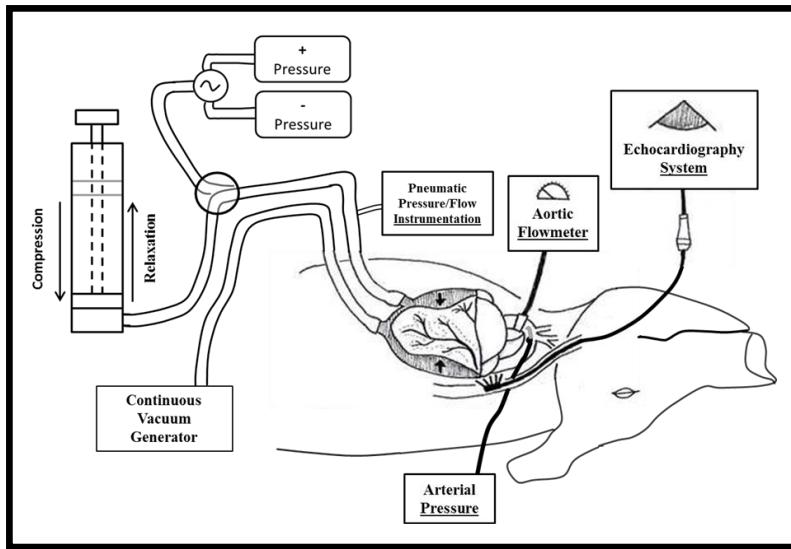
Data was acquired using the manually driven hand pump in comparison to ST system to identify optimal support dynamics.



Optimal dynamics during hand pump support were verified as similar to the optimal hemodynamics during ST support. Combined drive support analysis was used to set-up in-vivo testing.

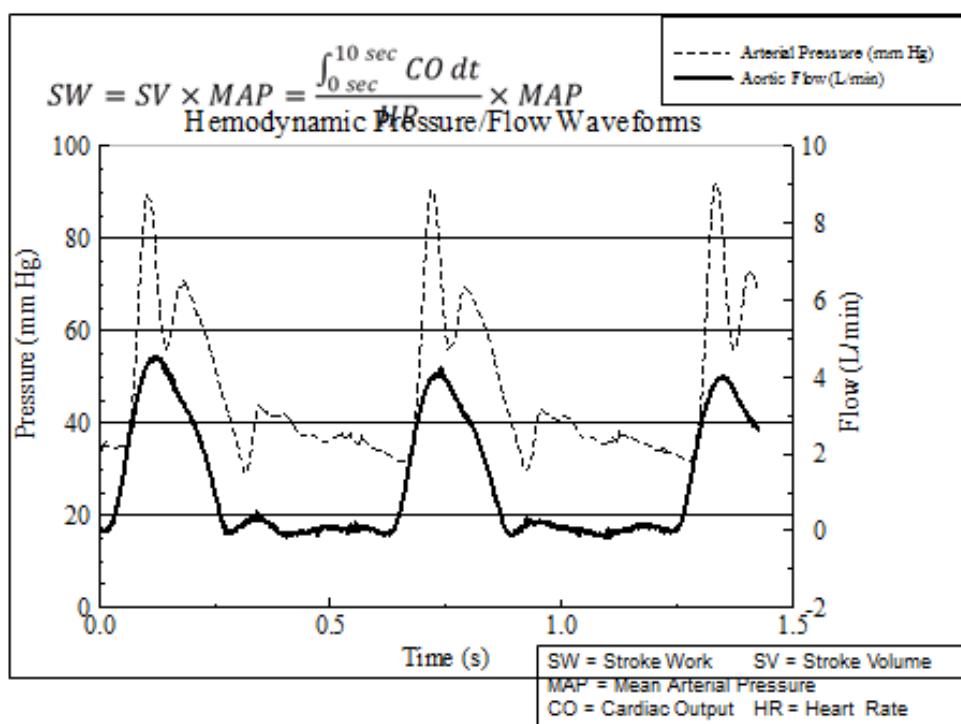
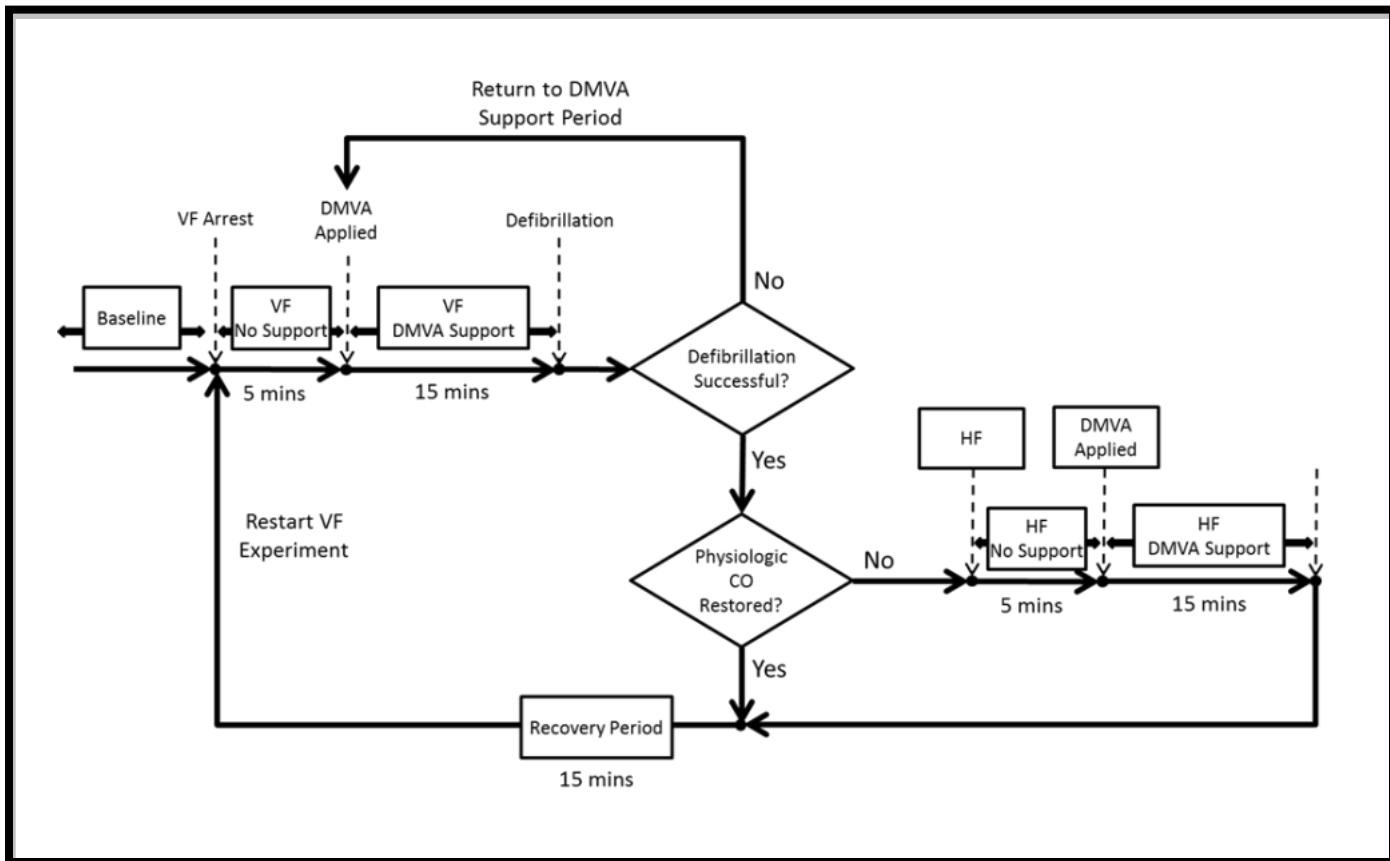


In-vivo testing used both large ovine and canine to represent clinically relevant heart sizes with the pig representative of an average adult heart:

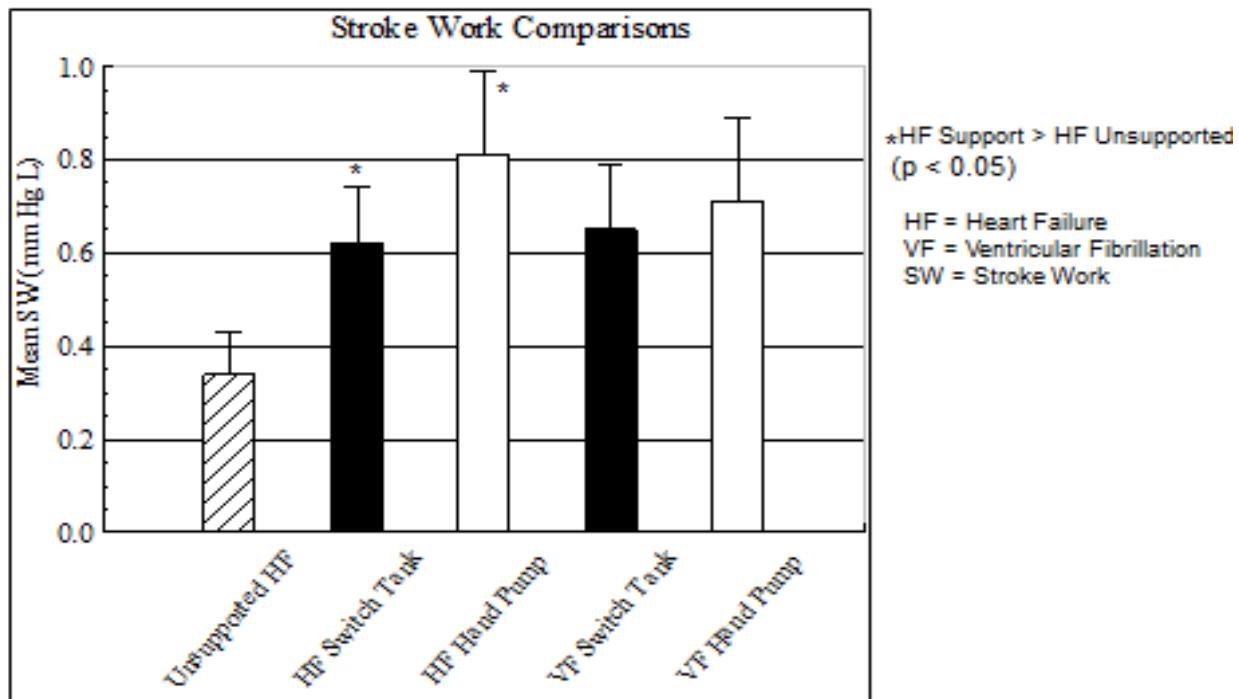


The below support algorithm was utilized to obtain support data during periods of cardiac arrest as well as varied degrees of cardiac failure during the animal experiments.

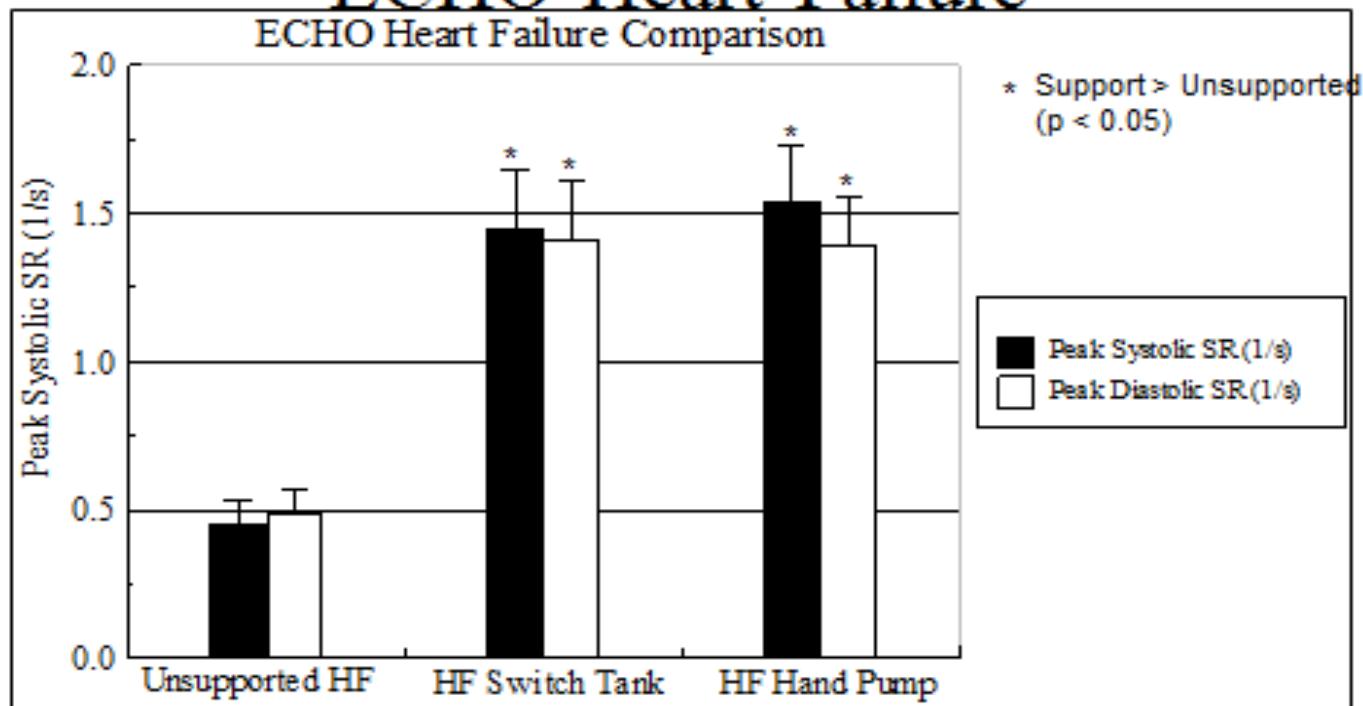
Data was collected on the custom data acquisition system to compare hemodynamics between different states of support and identify optimal drive characteristics of the HP.



# Stroke Work Calculations

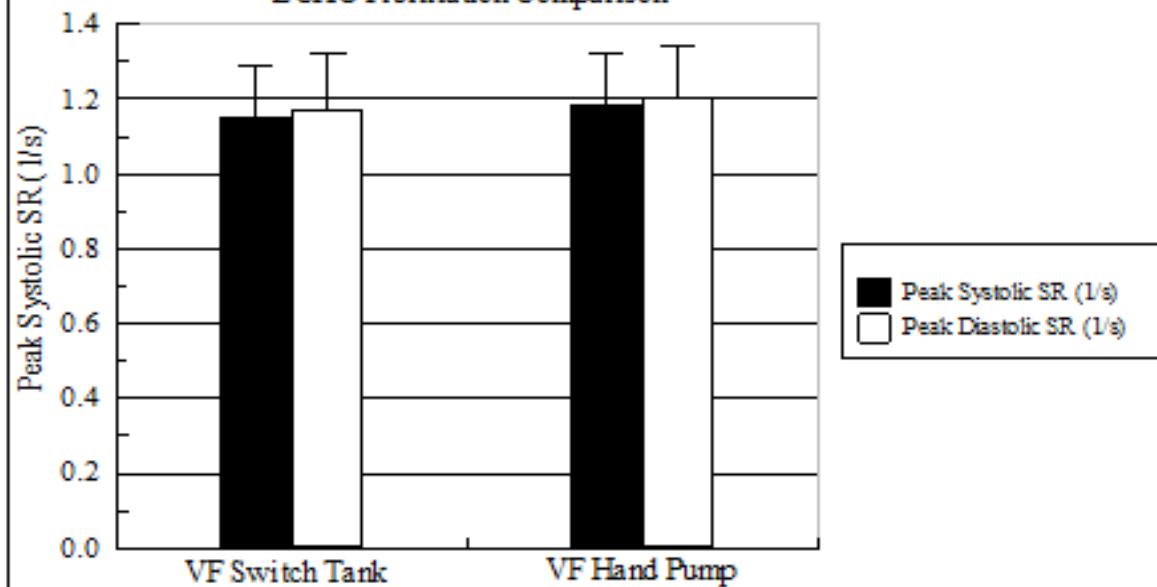


# ECHO Heart Failure



# ECHO Fibrillation

## ECHO Fibrillation Comparison



Requirements for powering the hand pump were thereby developed

## Pneumatic Drive Requirements for Direct Mechanical Ventricular Actuation



BA Schmitz<sup>1</sup>, KM Svatikamiller<sup>1</sup>, DB Reynolds<sup>2</sup>, RJ Danner<sup>2</sup>, RA Perez-Tamayo<sup>3</sup>, MP Anstalder<sup>4</sup>

<sup>1</sup>Departments of Mechanical, Industrial, & Nuclear, and Biomedical Engineering, Wright State University, Dayton, OH,

<sup>2</sup>Departments of Surgery, Wright State University, Dayton, OH, USA



SCHOOL OF MEDICINE  
WRIGHT STATE UNIVERSITY

COLLEGE OF  
ENGINEERING AND COMPUTER SCIENCE

Wright State University

### Abstract

Currently available mechanical circulatory support devices have complications related to blood coagulation. Direct Mechanical Ventricular Assistance (DMVA) utilizes a polymeric mesh placed over the ventricular myocardium to provide mechanical assistance against diastolic collapse. A pneumatic drive is used to expand and relax a noninvasive air pocket, defining systolic and diastolic ventricular function. The purpose of this study was to determine power requirements of a pneumatic drive for DMVA support.

Diastolic pump was constructed, undergoes assembly, and measurement of DMVA drive requirements. The assembly was then disassembled and reassembled. The diastolic and systolic pump volumes in the DMVA were measured. A diastolic pump pressure of 100 mmHg and a systolic pump pressure of 160 mmHg were used. The DMVA drive system was instrumented for pressure (Dynamax, 147 PCD-02) and flow (Flow Ratiotec, Model

### Materials and Methods

Ventilators (Siemens 5000, 6000, 8000) were purchased and instrumented. For hemodynamics monitoring and echocardiography, Median sternotomy was performed and heart was supported by DMVA during both circulation and failure. Both an automated resuscitator and manual hand pump pneumatic drive were used for DMVA support. The DMVA drive line was instrumented for pressure (Dynamax, 147 PCD-02) and flow (Flow Ratiotec, Model

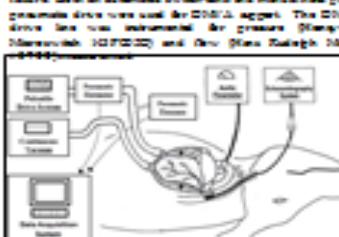
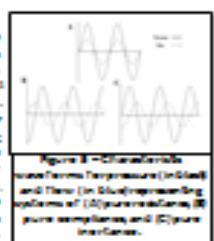


Figure 2 - Schematic of the system for direct mechanical ventricular actuation using a pneumatic drive.

This was recorded using National Instruments LabVIEW software at ten second intervals. The maximum magnitude and root-mean-square (RMS) pressure and flow was measured during experimental conditions. RMS flow (Q<sub>avg</sub>) and pressure (P<sub>avg</sub>) were used to calculate average apparent power for data analysis.

DMVA power requirements for systolic and diastolic assistance have not been previously shown or used. Therefore, the power requirements determined in this study will include the energy required to run an actuation drive. The efficiency of a drive system will determine such additional energy requirements.

Diastolic requirement for systolic and diastolic apparent power is the magnitude of a single drive stroke, which has real and reactive components. Real power requirement was calculated by taking resistance in flow. The reactive power relates to effects of air compliance, such as stroke in ventricle volume, and the air mass due to diastolic changes in



### Discussion

### Introduction

Direct Mechanical Ventricular Assistance is a ventricular assist device utilizing a polymeric mesh placed over the ventricular myocardium that augments ventricular function. While a diastolic compression device only provides systolic support (DMVA), this augments diastolic function.<sup>1</sup>



### Purpose

Recent work has focused on the power requirements for DMVA support of the patient ventricle heart.<sup>2,3</sup> The purpose of this study was to better understand the power requirements for DMVA support of the ventricle heart, with characterization of both systolic and diastolic requirements.

### Results



Figure 5 - Power Requirements (W) versus Time (s) for the pneumatic system. The table displays average power requirements for both systolic and diastolic assistance. There was no statistically significant difference between systolic vs. diastolic assistance ( $p = 0.20$ ). DMVA had a maximum power requirement of 1622 W and a minimum power requirement of 1022 W.

### Conclusion

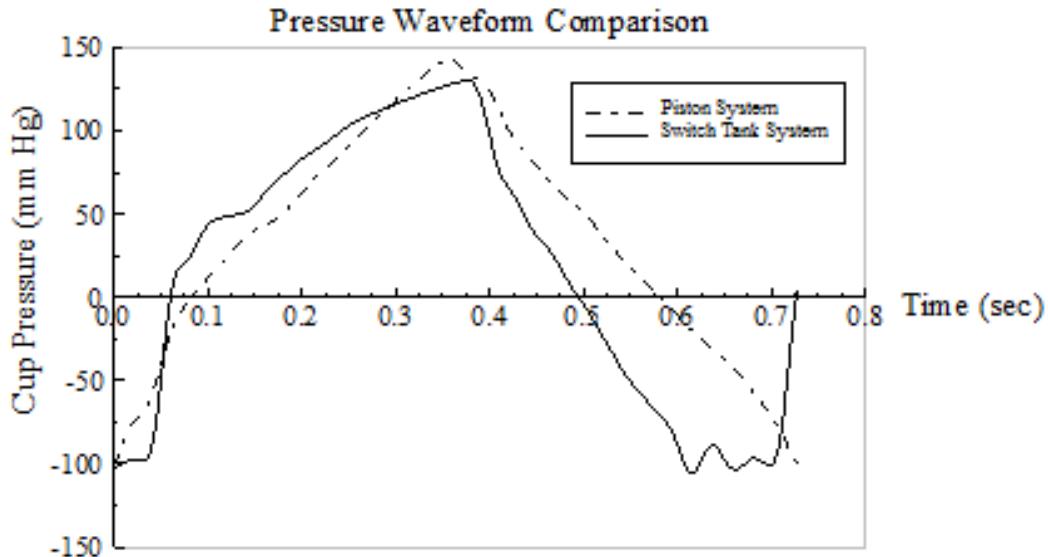
1. Power requirements for systolic and diastolic assistance are similar during DMVA support.
2. The power requirements for a pneumatic drive system must consider additional energy required for both systolic and diastolic assistance.
3. Future work will focus on developing an efficient and compact automated drive for DMVA support.

### References

- [1] Anstalder, M.P., Danner, R.J., Danner, R.J., Svatikamiller, K.M., Reynolds, D.B., Perez-Tamayo, R.A., and Schmitz, B.A. "Ventricular Assistance Reduces Systolic and Diastolic Myocardial Work in the Small Calfling Heart." *Journal of Biomechanics*, 32, 1023-1028, 2000.
- [2] Schmitz, B.A., Reynolds, D.B., Teitel, N., Callahan, J.J., George, E.M., Svatikamiller, K.M., and Anstalder, M.P. "Developing Systolic Systolic Assistance for Diastolic Mechanical Ventricular Assistance Systems." In 2002 Biomedical Engineering Society Annual Meeting, 2002 October 2002, St. Louis, MO.

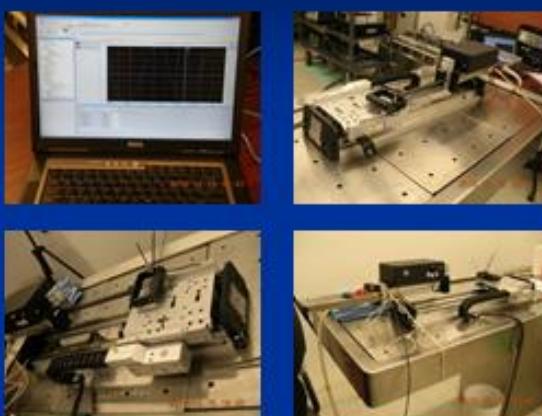
Proprietary interrogation of waveforms was also utilized for these exercises.

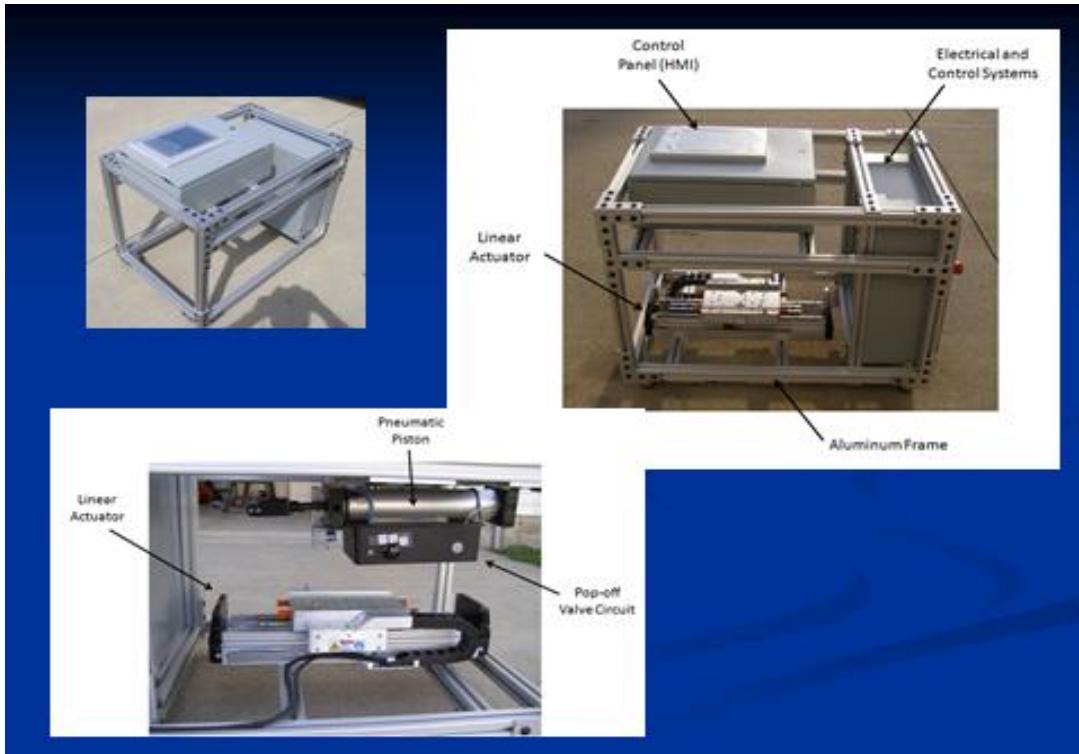
## Drive System Pressure Waveforms



A linear actuator was selected for the first prototype drive:

## Construction of Piston Drive

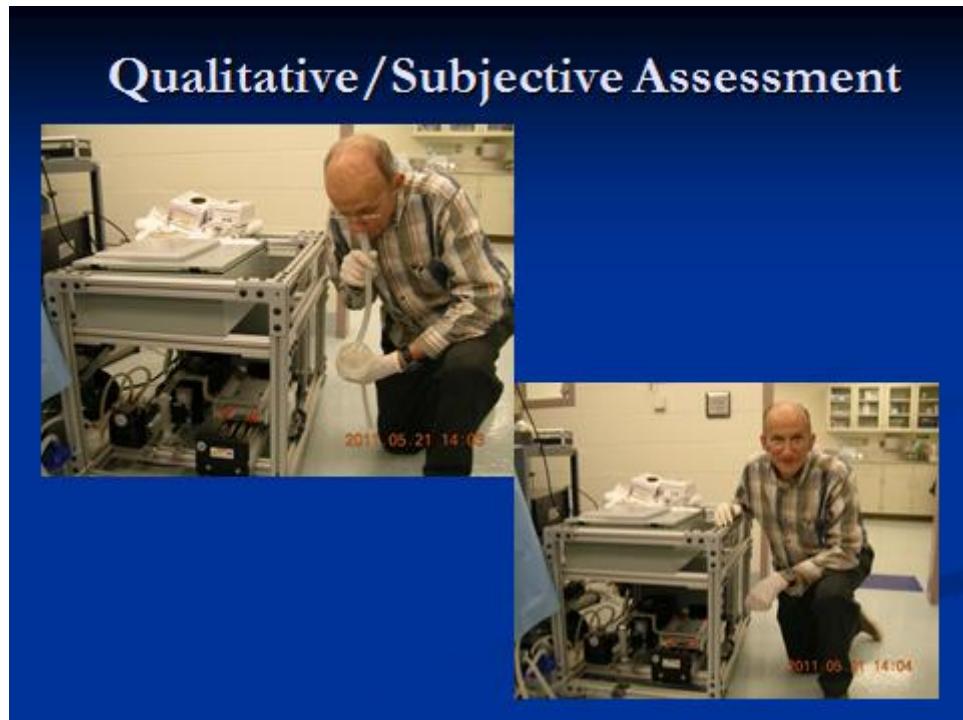




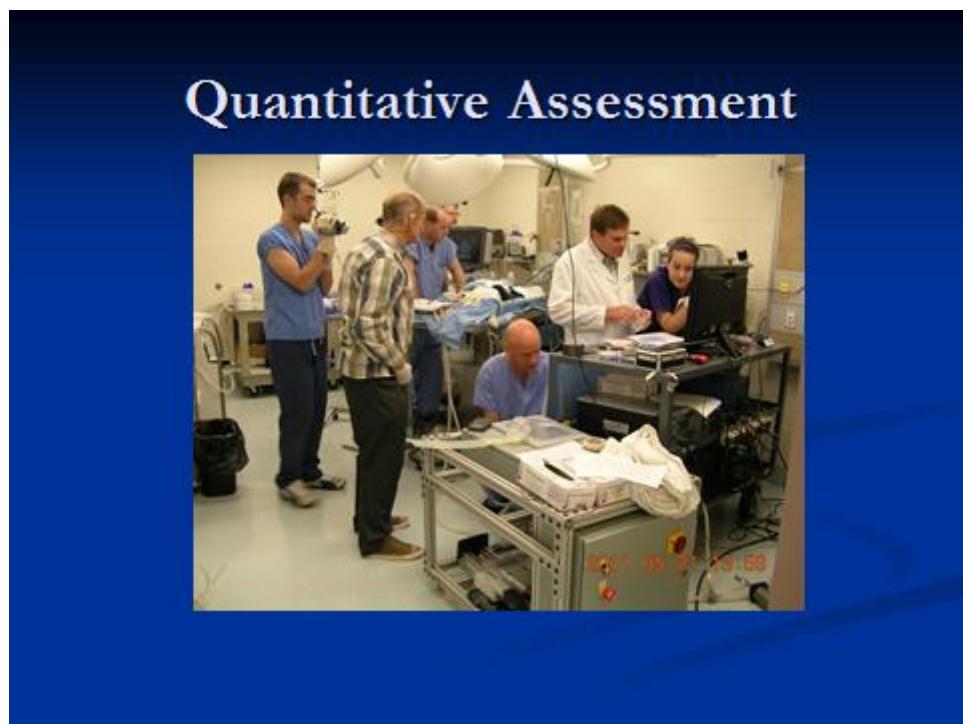
The initial system was housed along with all control components



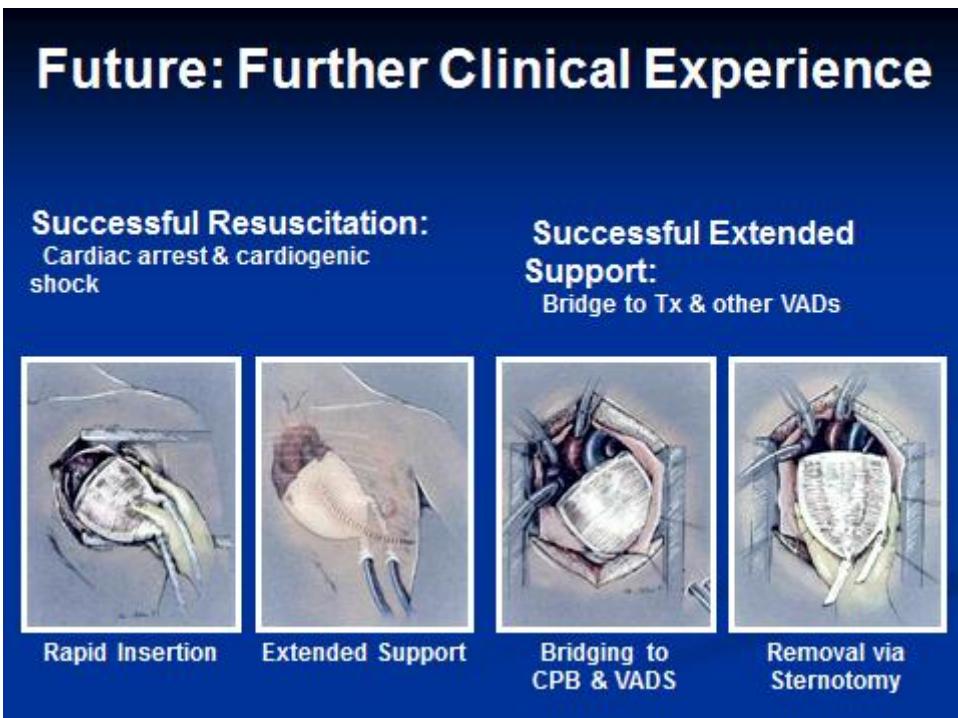
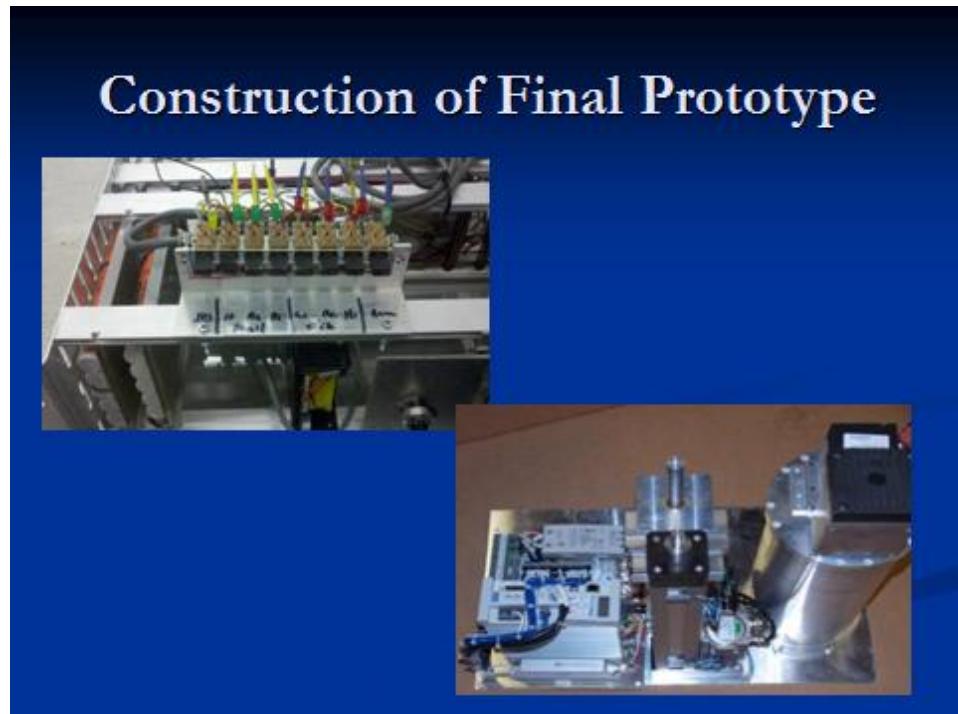
Dr. George L. Anstadt provided insight regarding quality control of all fabricated cups as well as additional verification pertaining to idealized support dynamics during the experiments.



This included Dr. George L. Anstadt's oversight of device installation and optimal drive dynamics during animal experiments.



Data and performance assessments obtained from the initial prototype drive were analyzed to determine specifications for building the automated prototype drive:



## 9. OTHER ACHIEVEMENTS

Nothing to report.

## 10. REFERENCES

**Anstadt MP**, Malone MP, Brown GR, Nolan DS, Quinones JD, Anstadt GL. Direct Mechanical Ventricular Assistance Promotes Salvage of Ischemic Myocardium. *Trans Am Soc Artif Intern Organs* 1987;33:720-725.

Brown CB, Schleifer J, Jenkins J, Anstadt GL, Werman HA, Tallman RD, Ashton J, Hamli RL, **Anstadt MP**: Effect of Direct Mechanical Ventricular Assistance on Myocardial Hemodynamics During Ventricular Fibrillation. *Crit Care Med* 1989;17:1175-1180.

**Anstadt MP**, Hendry PJ, Plunkett MD, Menius JA, Lowe JE: Comparisons of Direct Mechanical Ventricular Actuation (DMVA) and Cardiopulmonary Bypass (CPB). *ASAIO Transactions* 1989;35:464-467.

**Anstadt MP**, Hendry PJ, Plunkett MD, Menius JA, Pacifico AD, Lowe JE: Mechanical Myocardial Actuation During Ventricular Fibrillation Improves Tolerance to Ischemia Compared to Cardiopulmonary Bypass. *Circulation* 1990;82(5):IV-284-290.

**Anstadt MP**, Hendry PJ, Plunkett MD, Menius JA, Pacifico AD, Lowe JE. Mechanical Cardiac Actuation Achieves Hemodynamics Similar to CPB. *Surgery* 1990;108:442-451.

**Anstadt MP**, Bartlett RL, Malone JP, Brown GR, Martin S, Nolan DJ, Oberheu KH, Anstadt GL. Direct Mechanical Biventricular Actuation for Cardiac Arrest in Humans. *CHEST* 1991;100(1):86-92.

**Anstadt MP**, Anstadt GL, Lowe JE. Direct Mechanical Ventricular Actuation: A Review. *Resuscitation* 1991;21(1):7-23.

**Anstadt MP**, Taber JE, Hendry PJ, Plunkett MD, Tedder M, Menius JA, Jr., Lowe JE. Myocardial Tolerance to Ischemia After Resuscitation: Direct Mechanical Ventricular Actuation Versus Cardiopulmonary Bypass. *ASAIO Transactions* 1991;37:M518-519.

**Anstadt MP**, Stonnington, MJ, Tedder M, Crain BJ, Brothers MF, Hilleren DJ, Rahiha RJ, Menius JA, Jr., Lowe JE. Pulsatile Reperfusion After Cardiac Arrest Improves Neurologic Outcome. *Annals of Surgery* 1991;214(4):478-490.

Lowe JE, **Anstadt MP**, Van Trigt P, Smith PK, Hendry PJ, Plunkett MD, Anstadt GL. First Successful Bridge to Cardiac Transplantation Using Direct Mechanical Ventricular Actuation. *Annals of Thoracic Surgery* 1991;52:1237-1245.

**Anstadt MP**, Tedder SD, Vander Heide RS, Tedder M, Hilleren DJ, Sostman HD, Reimer KA, Menius JA, Lowe JE. Cardiac Pathology Following Resuscitative Circulatory Support: Direct Mechanical Ventricular Actuation Versus Cardiopulmonary Bypass. *ASAIO J* 1992;38(2):75-81.

Griffith RF, **Anstadt MP**, Hoekstra J, Van Ligten PF, Anstadt GL, Mitchell L, Brown CG. Regional Cerebral Blood Flow With Manual Internal Cardiac Massage Versus Direct Mechanical Ventricular Actuation. *Annals of Emergency Medicine* 1992;21(2):137-141.

**Anstadt MP**, Lowe JE: Reply, To the Editor: Direct Mechanical Ventricular Actuation. *Ann Thorac Surg* 1993;55:198-199.

**Anstadt MP**, Tedder M, Hegde SS, Perez-Tamayo RA, Crain BJ, Ha VLK, Abdel-aleem S, White WD, Lowe JE. Pulsatile Reperfusion Improves Cerebral Blood Flow Compared to Nonpulsatile Reperfusion Following Cardiac Arrest. *Ann Thorac Surg* 1993;56(3):453-461.

**Anstadt MP**, Perez-Tamayo RA, Banit DM, Walthall HP, Cothran, RL, Abdel-aleem S, Anstadt GL, Jones PL, Lowe JE. Myocardial Tolerance to Mechanical Actuation is Affected by Biomaterial Characteristics. *ASAIO J* 1994;40:M329-334.

Perez-Tamayo RA, **Anstadt MP**, Cothran Jr, LC, Reisinger, RJ, Schenkman, DI, Hulette C, Reimer KA, Anstadt GL, Lowe JE. Prolonged Total Circulatory Support Using Direct Mechanical Ventricular Actuation. *ASAIO J* 1995;41:M512-517.

Idriss SF, **Anstadt MP**, Anstadt GL, Ideker RE: The Effect of Cardiac Compression on Defibrillation Efficacy and the Upper Limit of Vulnerability. *J Cardio Electrophysiology* 1995;6: 368-378.

**Anstadt MP**, Perez-Tamayo RA, Davies MG, Hagen PO, St-Louis JS, Hendrickson SC, Abdel-aleem S, Reimer KA, Anstadt GL, Lowe JE. Experimental Aortocoronary Saphenous Vein Graft Function After Mechanical Cardiac Massage with the Anstadt Cup. *ASAIO J* 1996;42:295-300.

**Anstadt MP**, Schulte-Eistrup SA, Motomura T, Soltero E, Takano T, Mikati IA, Nonaka K, Joglar F, Nosé Y. Non-Blood Contacting Biventricular Support Synchronized to the Failing Heart. *Ann Thor Surg* 2002;73:556-562.

**Anstadt MP**, Budharaju S, Darner RJ, Schmitt BA, Prochaska LJ, Pothoulakis AJ, Portner PM. *Ventricular Actuation Improves Systolic and Diastolic Myocardial Function in the Small Failing Heart*, *Annals Thorac Surg* 2009;88:1982-8.

McConnell PI, **Anstadt MP**, del Rio CL, Preston T, Ueyama Y, Youngblood B. *Cardiac Function after Acute Support with Direct Mechanical Ventricular Actuation in Chronic Heart Failure*. In PRESS: ASAIO 2014.

## 11. APPENDICES

### CURRICULUM VITAE:

#### MARK P. ANSTADT, MD

##### **Professor, Department of Surgery**

Boonshoft School of Medicine, Wright State University  
[mark.anstadt@wright.edu](mailto:mark.anstadt@wright.edu)

##### **President, Miami Valley Heart & Lung Surgeons, LLC**

30 E. Apple St., Suite 6252, Dayton, OH 45409  
937.208.6060 o  
937.208.6061 f  
[mpanstadt@aol.com](mailto:mpanstadt@aol.com)

---

#### EDUCATION

The Pennsylvania State University State College, Pennsylvania	Animal Biosciences	B.S., 1982
Wright State University School of Medicine Dayton, Ohio	Medicine	M.D., 1986

#### POSTGRADUATE TRAINING

The Ohio State University Hospitals, Columbus, Ohio		
Intern	General Surgery	1986-1987
Resident	General Surgery	1987-1988
Duke University Medical Center, Durham, NC		
Research Fellow	Cardiothoracic Surgery	1988-1993
Resident	General Surgery	1993-1995
Chief Resident	General Surgery	1995-1996
Clinical Fellow	Cardiothoracic Surgery	1996-1997
Teaching Scholar	Cardiothoracic Surgery	1997-1998
Wright State University School of Graduate Studies	Healthcare Management Certificate	Jan -Dec 2013

#### CLINICAL APPOINTMENTS

Miami Valley Hospital	Vice- Chairman Department of Surgery Chairman, Section of Cardiothoracic Surgery Vice Chairman Section of Cardiothoracic Surgery Chairman Department of Surgery Vice Chairman Department of Surgery Medical Director Cardiothoracic Surgery Chief of Staff - Nominee	Jun 2014-Present May 2007-June 2014 Jun 2004-May 2007 Jun 2008-Jun 2010 Jun 2006-Jun 2008 Dec 2004-April 2012 Jul 2011
Upper Valley Medical Center Troy, OH	Chief Cardiovascular & Thoracic Section	Jun 2008-Present
VA Medical Center Dayton, OH	Consultant - Thoracic Surgeon	Apr 2004-Present
The Medical College of Georgia, Augusta, GA Section of Cardiothoracic Surgery Thoracic Surgery Training Program	Chief Director Associate Director	Jun 2002-Jul 2003 May 2002-Aug 2003 Jul 2000-May 2002

## ACADEMIC APPOINTMENTS

Wright State University, Dayton, OH Department of Surgery	Professor Associate Professor	Jul 2011-Present Apr 2004-Jun 2011
Department of Pharmacology & Toxicology Department of Graduate Studies	Adjunct, Associate Professor Associate Graduate Faculty	Apr 2006-Present Nov 2005-Present
The Medical College of Georgia, Augusta, GA Department of Surgery Department of Pharmacology & Toxicology Vascular Biology Center	Assistant Professor Assistant Professor Associate Member	Jul 2000-Jun 2004 Dec 2001-Jun 2004 Jan 2001-Jun 2004
Baylor College of Medicine, Houston, TX The Michael E. DeBakey Dept of Surgery	Assistant Professor	Jul 1998-Jul 2000

## CERTIFICATIONS

Diplomat, The American Board of Surgery Recertification	Dec 1997 Dec 2007
Diplomat, The American Board of Thoracic Surgery Recertification	Jun 1999 Dec 2007
ACLS	
ATLS	
ATLS	

## MEDICAL LICENSURE

State of Ohio  
State of NC  
State of Georgia  
State of Illinois

## MILITARY SERVICE

U.S. Army Reserves Medical Corps  
Colonel, 4005<sup>th</sup> U.S. Army Hospital, Houston, TX  
Mar 1987-Present

## PROFESSIONAL MEMBERSHIP

American Medical Association	1984-Present
American Society for Artificial Internal Organs	1986-Present
FACS, American College of Surgeons	1997-Present
David C. Sabiston, Surgical Society	1998-Present
Michael E. DeBakey International Surgical Society	1999-Present
Society of Thoracic Surgeons	1999-Present
American College of Surgeons Oncology Group	2000-Present
Southern Thoracic Surgical Association	2002-Present
FACCP, American College of CHEST Physicians	2002-Present
American Thoracic Society	2003-Present
American Heart Association	2005-Present

## PATENTS

<i>Sensor-Equipped and Algorithm-Controlled Direct Mechanical Ventricular Assist Device</i>	Issued: Oct 2008
<i>Method and Appatus for Minimally Invasive Direct Mechanical Ventricular Actuation</i>	Issued: Jun 2010

## GRANTS & AWARDS

American Heart Association, Miami Valley Chapter	May 1985-May 1986
Research Grant Investigating DMVA during Ischemic Reperfusion	
Wright State University School of Medicine Research Grant	Apr 1985
<i>An Evaluation of DMVA on Myocardial Infarct Size in an Occlusion-Reperfusion Model</i>	
Wright State University School of Medicine	Sep 1985
Golden Speculum Award for Excellence in Obstetrics & Gynecology	
Wright State University School of Medicine	Jun 1986
Upjohn Achievement Award	
The Ohio State University School of Medicine	Jun 1988
House Staff Teaching Award	
NIH, National Research Service Award	Aug 1988-Aug 1990
<i>Investigating Mechanical Actuation of the Heart</i>	
The American Society for Artificial Internal Organs	May 1989
Travel Fellowship Award	
McGill University	Oct 1990
Heward Visiting Scientist Fellowship	
Nippon Zeon Research Grant	Jan 1991
<i>Investigating DMVA: Perfusion during Regional Myocardial Ischemia and Reperfusion</i>	
Upjohn Research Grant	Apr 1991
<i>Investigation Lazaroids for Resuscitation</i>	
NIH, Cardiovascular Research Grant	Jul 1991-Jul 1993
<i>Investigating Mechanical Actuation of the Heart: Laboratory and Clinical Studies,</i>	
Collaborating Investigator, NIH Project Grant	Jul 1992-Jul 1995
<i>Non-Blood Contacting Biventricular Support Co-PI, American Diabetes Association Research Award</i>	
<i>Role of Endothelin-1 Activation in Vascular Complications of Diabetes</i>	Jul 1999-Jun 2002

PI, Medical College of Georgia Research Award <i>Endothelin Activation in Coronary Artery Grafting Surgery,</i>	Oct 2001-Jun 2003
Co-PI, ONS Foundation Grant Research Award <i>Symptoms of Post Surgical Patients with Lung Cancer,</i>	Oct 2002-Sep 2003
Co-PI, American Diabetes Association Research Award <i>Endothelin-1 and Vascular Mediated Remodeling in Diabetes,</i>	Jan 2003-Dec 2005
PI, Research & Development Funding, Myotech, LLC <i>Developing Small Animal Models,</i>	Jun 2004-Oct 2008
Outstanding Alumni Award Boonshoft School of Medicine, Wright State University, Dayton, OH	Feb 7, 2009
PI, DOD Contract No. W81XWH-08-1-0484 <i>New Heart Failure Treatment Capability for Remote Environments,</i>	May 2009-Jun 2013

## RECENT COMMITTEE ACTIVITY

Miami Valley Hospital	Cancer Committee	2011-Present
	WSU Dept Surgery, Research Committee	2009-Present
	Medical Staff Executive Committee	2008-2010
	Endoscopy Committee	2008-Present
	Operating Room Committee	2007-Present
	Endovascular Stent Committee	2006-Present
	Trauma Committee	2006-Present

## INDUSTRY RELATED ACTIVITIES

Consultant - SMEC, Inc., Cookeville, TN Intra-aortic Balloon Pump & Internal Defibrillator R&D and Fabrication	1976-1982
Consultant - Applied Sciences Inc, Dayton, OH Medical Devices; R&D	1982-1988
Vice President - Advanced Resuscitation Innovations, Inc, Dayton, OH Medical Devices/R&D	1992-1996
Chair, Industry Speaks Session <i>Cups, Sacs, Spinners, and Rollers--Simpler Methods of Circulatory Support</i> , 39th Annual Meeting of ASAIO	1992-1993
Consultant - Williamson Advisors Inc, Atlanta, GA Medical Products Ventures	1994-2003
Consultant & Member Board of Directors - Cardio Technologies Inc, New York, NY DMVA R&D	1996- 2000
Medical Director, Consultant & Member Board of Directors - Myotech, Pittsford, NY DMVA R&D	2003-2008
President - LifeBridge Technologies, LLC, Pittsford, NY DMVA R&D	2008-Present

## CHAPTERS

**Anstadt MP:** Cardiac Assist Devices and the Artificial Heart. In ESSENTIALS OF SURGERY, Sabiston & Lyerly (eds) Second Edition: 738-746, 1994.

**Anstadt MP**, Lowe JE: The Coronary Circulation: Surgical Management of Coronary Artery Disease: Assisted Circulation, In SURGERY OF THE CHEST, Sixth Edition, Sabiston & Spencer (eds): 1995-2017, 1995.

**Anstadt MP**, Perez-Tamayo RA, Lowe JE, Anstadt GL: Recent Progress Using the Anstadt Cup for Direct Mechanical Ventricular Actuation, In ASSISTED CIRCULATION 4, Felix Unger (ed): 394-408, 1995.

**Anstadt MP**, Newman MF: Use of the Intra-aortic Balloon Pump for Post-Cardiotomy Support. In INTRA-AORTIC BALLOON PUMP THERAPY, Maccioli (ed): 107-125, 1996.

Lucas WA, **Anstadt MP**: Triggering and Timing of the Intra-aortic Balloon Pump. In INTRA-AORTIC BALLOON PUMP THERAPY, Maccioli (ed): 57-68 1996.

**Anstadt MP**, Lowe LE: Cardiopulmonary Resuscitation. In CARDIAC SURGERY IN THE ADULT, Cohn (ed), 2<sup>nd</sup> Edition: 471-494, 2003.

**Anstadt MP**, Lowe LE: Cardiopulmonary Resuscitation. In CARDIAC SURGERY IN THE ADULT, Cohn (ed), 3<sup>rd</sup> Edition: 487-506, 2007.

**Anstadt MP**, Lowe LE: Cardiopulmonary Resuscitation. In CARDIAC SURGERY IN THE ADULT, Cohn (ed), 4<sup>th</sup> Edition, 401-416, 2011; McGraw-Hill, New York, NY.

THE ADULT,

## SCIENTIFIC PUBLICATIONS

Anstadt GL, Schiff P, **Anstadt MP**. Umbrella Balloon for Maximum Unloading During Intra-Aortic Balloon Pumping. Trans Am Soc Artif Intern Organs 1981;27:461- 466.

**Anstadt MP**, Malone MP, Brown GR, Nolan DS, Quinones JD, Anstadt GL. Direct Mechanical Ventricular Assistance Promotes Salvage of Ischemic Myocardium. Trans Am Soc Artif Intern Organs 1987;33:720-725.

Brown CB, Schleifer J, Jenkins J, Anstadt GL, Werman HA, Tallman RD, Ashton J, Hamli RL, **Anstadt MP**: Effect of Direct Mechanical Ventricular Assistance on Myocardial Hemodynamics During Ventricular Fibrillation. Crit Care Med 1989;17:1175-1180.

**Anstadt MP**, Hendry PJ, Plunkett MD, Menius JA, Lowe JE: Comparisons of Direct Mechanical Ventricular Actuation (DMVA) and Cardiopulmonary Bypass (CPB). ASAIO Transactions 1989;35:464-467.

Hendry PJ, Packer DL, **Anstadt MP**, Plunkett MD, Lowe JE. Surgical Treatment of Automatic Atrial Tachycardia. Presented at the 25th Anniversary Meeting of the Society of Thoracic Surgeons, Baltimore, MD, Annals of Thoracic Surgery 1990;49:253-260.

**Anstadt MP**, Hendry PJ, Plunkett MD, Menius JA, Pacifico AD, Lowe JE: Mechanical Myocardial Actuation During Ventricular Fibrillation Improves Tolerance to Ischemia Compared to Cardiopulmonary Bypass. Circulation 1990;82(5):IV-284-290.

**Anstadt MP**, Hendry PJ, Plunkett MD, Menius JA, Pacifico AD, Lowe JE. Mechanical Cardiac Actuation Achieves Hemodynamics Similar to CPB. Surgery 1990;108:442-451.

Hendry PJ, **Anstadt MP**, Plunkett MD, Pacifico AD, Jr., Mikat EM, Menius JA, Jr., Lowe JE. The Optimal Temperature for Preservation of Donor Myocardium. Circulation 1990;82(5):IV-306-312.

**Anstadt MP**, Bartlett RL, Malone JP, Brown GR, Martin S, Nolan DJ, Oberheu KH, Anstadt GL. Direct Mechanical Biventricular Actuation for Cardiac Arrest in Humans. CHEST 1991;100(1):86-92.

**Anstadt MP**, Anstadt GL, Lowe JE. Direct Mechanical Ventricular Actuation: A Review. Resuscitation 1991;21(1):7-23.

**Anstadt MP**, Taber JE, Hendry PJ, Plunkett MD, Tedder M, Menius JA, Jr., Lowe JE. Myocardial Tolerance to Ischemia After Resuscitation: Direct Mechanical Ventricular Actuation Versus Cardiopulmonary Bypass. ASAIO Transactions 1991;37:M518-519.

**Anstadt MP**, Stonnington, MJ, Tedder M, Crain BJ, Brothers MF, Hilleren DJ, Rahiha RJ, Menius JA, Jr., Lowe JE. Pulsatile Reperfusion After Cardiac Arrest Improves Neurologic Outcome. Annals of Surgery 1991;214(4):478-490.

Lowe JE, **Anstadt MP**, Van Trigt P, Smith PK, Hendry PJ, Plunkett MD, Anstadt GL. First Successful Bridge to Cardiac Transplantation Using Direct Mechanical Ventricular Actuation. Annals of Thoracic Surgery 1991;52:1237-1245.

Amato MT, Hendry PJ, **Anstadt MP**, Plunkett MD, Taber JE, Lowe JE. Effects of Amiodarone Versus Dobutamine on Subsequent Tolerance to Global Myocardial Ischemia. *Surgical Forum XLII*, peripheral pulses are equal and adequate throughout, no significant JVD or edema 1991;253-254.

**Anstadt MP**, Tedder SD, Vander Heide RS, Tedder M, Hilleren DJ, Sostman HD, Reimer KA, Menius JA, Lowe JE. Cardiac Pathology Following Resuscitative Circulatory Support: Direct Mechanical Ventricular Actuation Versus Cardiopulmonary Bypass. *ASAIO J* 1992;38(2):75-81.

Hendry PJ, **Anstadt MP**, Plunkett MD, Amato MT, Menius JA, Lowe JE. Improved Donor Myocardial Recovery Using a New Lipid Anti-Peroxidant. *J. Heart Lung Transplant* 1992;11:636-645

Griffith RF, **Anstadt MP**, Hoekstra J, Van Ligten PF, Anstadt GL, Mitchell L, Brown CG. Regional Cerebral Blood Flow With Manual Internal Cardiac Massage Versus Direct Mechanical Ventricular Actuation. *Annals of Emergency Medicine* 1992;21(2):137-141.

Tedder M, **Anstadt MP**, Tedder SD, Lowe JE: Current Morbidity, Mortality and Survival Following Bronchoplastic Procedures. *Annals of Thoracic Surgery* 1992;54:387-391.

Tedder M, **Anstadt MP**, Wharton JM, Revishvili A, Hegde SS, Lowe JE: Prophylactic Implantable Defibrillator Patches in Patients at High Risk for Malignant Ventricular Dysrhythmias. *ASAIO Journal* 1992;38:M261-265.

**Anstadt MP**, Tedder M, Hegde SS, Douglas JM, Sperling RT, White WD, Van Trigt P, Lowe JE: Intraoperative Timing May Provide Criteria for Postcardiotomy Assist Device Utilization. *ASAIO J* 1992;38:M147-150.

Duhaylongsod FG, **Anstadt MP**, Tedder M, Crawford FA, Jr., Wolfe WG, Lowe JE: Depletion of the Ventricular Mitochondrial Oxygen Store: The Etiology of Tachycardia-Induced Cardiomyopathy. *Surgical Forum XLIII*, peripheral pulses are equal and adequate throughout, no significant JVD or edema. 1992;257-260.

Hendry PJ, Mikat EM, **Anstadt MP**, Plunkett MD, Lowe JE: Argon Beam Coagulation Compared with Cryoablation of Ventricular Subendocardium. *Ann Thorac Surg* 1993;55:135-139.

Tedder M, Wharton JM, **Anstadt MP**, Revishvili ASh, Hegde SS, Lowe JE: Optimal Defibrillator Patch Configurations Include the Right Heart and Left Ventricle. *The Journal of Cardiology* 1993;71:349-350.

**Anstadt MP**, Lowe JE: Reply, To the Editor: Direct Mechanical Ventricular Actuation. *Ann Thorac Surg* 1993;55:198-199.

**Anstadt MP**, Tedder M, Hegde SS, Perez-Tamayo RA, Crain BJ, Ha VLK, Abdel-aleem S, White WD, Lowe JE. Pulsatile Reperfusion Improves Cerebral Blood Flow Compared to Nonpulsatile Reperfusion Following Cardiac Arrest. *Ann Thorac Surg* 1993;56(3):453-461.

Tedder M, **Anstadt MP**, Tedder, SD, Revishvili ASh, Hegde SS, Lowe JE. Sensing Lead Insulation Fractures Following Implantable Cardioverter-Defibrillator Placement. *ASAIO Journal* 1993;39:M711-M714.

Tedder M, Spratt JA, **Anstadt MP**, Hegde SS, Tedder SD, Lowe JE. Early Surgical Intervention Improves Survival in Patients with Pulmonary Mucormycosis. *Ann Thorac Surg* 1994;57:1044-1050.

Abdel-aleem S, Li X, **Anstadt MP**, Perez-Tamayo RA, Lowe JE. Regulation of Glucose Utilization During the Inhibition of Fatty Acid Oxidation in Rat Myocytes. *Horm metab Res* 1994;26:88-91.

Abdel-aleem S, Badr M, Perez-Tamayo RA, **Anstadt MP**, Lowe JE. Stimulation of Myocyte Insulin-Responsive Glucose Transporters By The Inhibition of Fatty Acid Oxidation. *Diabetes Research* 1993;22(1):9-11.

**Anstadt MP**, Perez-Tamayo RA, Banit DM, Walthall HP, Cothran, RL, Abdel-aleem S, Anstadt GL, Jones PL, Lowe JE. Myocardial Tolerance to Mechanical Actuation is Affected by Biomaterial Characteristics. *ASAIO J* 1994;40:M329-334.

Abdel-aleem S, Sharwi S, Sayed-Ahmed M, **Anstadt MP**, Lowe JE. Reduced Induction of Carbohydrate Utilization by Inhibition of Fatty Acid Oxidation in Myocytes from Diabetic Animals. *Horm. Metab. Res* 1995;27:104-106.

Perez-Tamayo RA, **Anstadt MP**, Cothran Jr, LC, Reisinger, RJ, Schenkman, DI, Hulette C, Reimer KA, Anstadt GL, Lowe JE. Prolonged Total Circulatory Support Using Direct Mechanical Ventricular Actuation. *ASAIO J* 1995;41:M512-517.

Plunkett MD, Hendry PJ, **Anstadt MP**, Camporesi EM, Amato MT, St. Louis JD, Lowe JE. Chronic Hypoxia Induces Adaptive Metabolic Changes in Neonatal Myocardium. *J Thor Card Surg* 1996;112 (1): 8-13.

Idriss SF, **Anstadt MP**, Anstadt GL, Ideker RE: The Effect of Cardiac Compression on Defibrillation Efficacy and the Upper Limit of Vulnerability. *J Cardio Electrophysiology* 1995;6: 368-378.

**Anstadt MP**, Perez-Tamayo RA, Davies MG, Hagen PO, St-Louis JS, Hendrickson SC, Abdel-aleem S, Reimer KA, Anstadt GL, Lowe JE. Experimental Aortocoronary Saphenous Vein Graft Function After Mechanical Cardiac Massage with the Anstadt Cup. *ASAIO J* 1996;42:295-300.

Anderson JE, Chang AS, **Anstadt MP**. Polytetrafluoroethylene Hemoaccess Site Infections. *ASAIO J* 2000;46(6):18-21.

**Anstadt MP**, Schulte-Eistrup SA, Motomura T, Soltero E, Takano T, Mikati IA, Nonaka K, Joglar F, Nosé Y. Non-Blood Contacting Biventricular Support Synchronized to the Failing Heart. *Ann Thor Surg* 2002;73:556-562.

Khanna SK, **Anstadt MP**, Bhimji S, Bannan MA, Mawulawde K, Zumbro GL, Moore HV. Apico-Aortic Conduits in Children with Severe Left Ventricular Outflow Tract Obstruction. *Ann Thoracic Surgery* 2002;73:81-87.

**Anstadt MP**, Gadacz TR. Esophagectomy, What Is the Best Approach? *Current Surgery* 2002;59(2):150-158.

Zumbro GL, Mawulawde K, Bhimji S, Paliotta, MA, **Anstadt MP**. Surgical Management of Esophageal Perforation: Role of Esophageal Conservation in Delayed Perforation. *The Amer Surg* 2002;68(1):36-40.

**Anstadt MP**, Carwile JM, Guill CK, Conklin LD, Soltero E, Lucci. Relapse of Thrombotic Thrombocytopenic Purpura Associated with Decreased vWF Cleaving Enzyme Activity. *Amer J Medical Sciences* 2002;323(5): 281-284.

Grubbs AL, **Anstadt MP**, Ergul A. Saphenous Vein Endothelin System Expression and Activity in African-American Patients. *Aterioscler Throb Vasc Biol* 2002;22: 1122-1127.

**Anstadt MP**, Hutchinson J, Portik-Dobos V, Jafri F, Bannan M, Mawulawde K, Ergul A. Vascular Endothelin Converting Enzyme-1 Expression and Activity is Upregulated in Clinical Diabetes. *Ethnicity & Disease* 2002;12(S3):5-9.

Mattke AF, Vender JR, **Anstadt MP**. Pituitary Apoplexy Presenting as Addisonian Crisis Following Coronary Artery Bypass Grafting. A Case Report & Literature Review. *Tex Heart Inst J* 2002;20: 193-199.

Mondy JS, **Anstadt MP**, Franga DL, Hutchinson J, Portik-Dobos V, Ergul A. Decreased Vascular Matrix Metalloproteinase Abundance in Diabetic Patients with Symptomatic Macroangiopathy. *Ethnicity & Disease* 2002;12(S3):18-22.

Portik-Dobos V, **Anstadt MP**, Hutchinson J, Bannan M, , Ergul A. Evidence for a Matrix Metalloproteinase Induction/Activation System in Arterial Vasculature and Decreased Synthesis and Activity in Diabetes. *Diabetes* 2002;51:3063-3068.

Lee JR, **Anstadt MP**, Khwaja S, Green LK: Gastrointestinal Stromal Tumor of the Esophagus. *European Journal of Cardio-thoracic Surgery* 2002;22:1009-1011.

**Anstadt MP**, Guill CK, Ferguson E, Gordon HS, Soltero E, Beall AC, Musher DM. Surgical versus Nonsurgical Treatment of Empyema Thoracis. An Outcomes Analysis. *The American Journal of Medical Sciences* 2003;326(1): 9-14.

**Anstadt MP**, Franga DL, Portik-Dobos V, Pennathur A, Hutchinson J, Bannan M, Mawulawde K, Ergul A. Native Matrix Metalloproteinase Characteristics May Influence Early Stenosis of Venous Versus Arterial CABG Conduits. *CHEST* 2004;125:1853-1858.

Williams HT, Gossage JR, Allred TJ, Kallab AM, Pancholy A, **Anstadt MP**. F-18-FDG PET Imaging of Rare Soft Tissue Sarcomas: Low-Grade Fibromyxoid Sarcoma and Malignant Hemangiopericytoma. Clinical Nuclear Medicine 2004; 29(9):581-584.

Ergul A, Johansen JS, Strømhaug C, Harris AK, Hutchinson J, Tawfik A, Rahimi A, Rhim E, Wells B, Caldwell RW, **Anstadt MP**. Vascular Dysfunction of Venous Bypass Conduits Is Mediated by Reactive Oxygen Species in Diabetes: Role of Endothelin-1. JPET 2005;313:70-77.

Takach TJ, **Anstadt MP**, Moore HV. Pediatric Aortic Disruption. Tex Heart Inst J 2005;32:16-20.

Straus JP, Woods RJ, McCarthy MC, **Anstadt MP**, Kwon N. Cardiac Pneumatic Nail Gun Injury. J Thorac Cardiovasc Surg 2006;132(3):702-3.

Wozniak CJ, Paull DE, Moezzi JE, Scott RP, Anstadt MP, York VV, Little AG. *Choice of First Intervention is Related to Outcomes in the Management of Empyema*. Ann Thorac Surg 2009;87:1525-31.

**Anstadt MP**, Budharaju S, Darner RJ, Schmitt BA, Prochaska LJ, Pothoulakis AJ, Portner PM. *Ventricular Actuation Improves Systolic and Diastolic Myocardial Function in the Small Failing Heart*, Annals Thorac Surg 2009;88:1982-8.

Kathula, S, Thomas D, **Anstadt MP**, Khan A. Paraneoplastic Cutaneous Leukocytoclastic Vasculitis and Iron Deficiency Anemia as the Presenting Features of Squamous Cell Lung Carcinoma. J Clin Oncology 2010, e83-e85.

Shewale SV, **Anstadt MP**, Horenziak M, Isu, B, Morgan EM, Lucot JB, Morris M. *Sarin Cause Autonomic Imbalance and Cardiomyopathy: An Important Issue for Military and Civilian Health*. Journal of Cardiovascular Pharmacology, 2012;July;60(1); 76-87.

Alghamri MS, Weir NM, **Anstadt MP**, Elased KM, Gurley SB, Morris M. *Enhanced Angiotensin II-Induced Cardiac and Aortic Remodeling in ACE2 Knockout Mice*. J Cardiovasc Pharmacol Ther. 2013 Mar;18(2):138-51.

McConnell PI, **Anstadt MP**, del Rio CL, Preston T, Ueyama Y, Youngblood B. *Cardiac Function after Acute Support with Direct Mechanical Ventricular Actuation in Chronic Heart Failure*. In PRESS: ASAIO 2014.

## ABSTRACTS

**Anstadt MP**, Bartlett RL, McCabe JB, Nolan DS, Anstadt GL: *Comparison of Closed and Open Chest Cardiac Compression with Direct Mechanical Ventricular Assistance*. Artif Organs 9:26, 1985.

Anstadt GL, **Anstadt MP**, Bartlett RL, McCabe JB, Nolan DS: *Comparison of Closed Chest and Open Chest Cardiac Compression with Direct Mechanical Ventricular Assistance*. Vet Surg 14:45-46,1985.

**Anstadt MP**, Galbraith TA, Murray KD, Howanitz EP, Myerowitz PD: *Bridge to Cardiac Transplantation Using Prosthetic Biventricular Circulatory Support*. The Society of Thoracic Surgeons, Abstract Book, Circulatory Support,1988.

**Anstadt MP**, Malone MP, Brown GR, Nolan DS, Quinones JD, Anstadt GL: *An Improved Method of Internal Cardiac Massage Promotes Salvage of Ischemic Myocardium*. (Extended Abstract) Curr Surg 45:195-198,1988.

**Anstadt MP**, Brown CG, Ligten PV, Anstadt GL, Neuman R: *Evaluation of Direct Mechanical Ventricular Assistance Following Fifteen Minutes of Ventricular Fibrillation in a Swine Model*. Annals of Emergency Medicine, 18(4):473,1989.

**Anstadt MP**, Hendry PJ, Plunkett MD, Menius JA, Pacifico AD, Lowe JE: *Mechanical Myocardial Actuation Improves Tolerance to Ischemia*. Circulation (Suppl II)80(4): II-318, Oct 1989.

**Anstadt MP**, Bartlett RL, Malone JP, Brown GR, Martin S, Nolan DS, Oberheu KH, Anstadt GL: *Biventricular Mechanical Cardiac Actuation in Humans*. Circulation (Suppl II) 80 (4): II-671, Oct 1989.

Griffith RF, **Anstadt MP**, Hoekstra J, Van Ligten P, Anstadt G, Casto L, Brown CG: *Effect of Direct Mechanical Ventricular Assistance Versus Open-Chest Cardiac Massage on Regional Cerebral Blood Flow in Swine*. Annals of Emergency Medicine 19(4):208,1990.

**Anstadt MP**, Stonnington MJ, Tedder M, Crain BJ, Hilleren DJ, Brothers MT, Rahija R, Menius JA, Jr., Lowe JE: *Pulsatile Reperfusion Following Cerebral Ischemia Improves Neurologic Outcome*. The American Surgical Association Program Book, Abstract #27, peripheral pulses are equal and adequate throughout, no significant JVD or edema. 83-85,1991.

**Anstadt MP**, Hendry PJ, Plunkett MD, Menius JA, Taber J, Tedder M, Lowe JE: *Biventricular Cardiac Assist vs. Cardiopulmonary Bypass (CPB) for Resuscitation*. The 37th Annual Meeting of the American Society of Artificial Internal Organs (ASAIO), Abstract Book 20:44,1991.

**Anstadt MP**, Tedder S, Tedder M, Vander Heide R, Hilleren DJ, Sostman D, Catena J, Reimer K, Menius JA, Lowe JE: *Lack of Myocardial Trauma Following Acute Biventricular Cardiac Actuation for Resuscitation*. The 37th Annual Meeting of the American Society of Artificial Internal Organs (ASAIO), Abstract Book 20:44,1991.

**Anstadt MP**, Tedder M, Douglas JM, Van Trigt P, Smith PK, Wolfe WG, Lowe JE: *Centrifugal Pump Circulatory Support Following Cardiac Surgery. Circulatory Support 1991, The Second International Conference on Circulatory Support Devices for Severe Cardiac Failure, Abstract Book, peripheral pulses are equal and adequate throughout, no significant JVD or edema*. DD,1991.

**Anstadt MP**, Tedder M, Stonnington, MJ, Taber JE, Crawford FA, Jr., Lowe JE: *Thermodilution Techniques Erroneously Predict Flow Alterations During Cardiac Failure*. JACC 19(3): 135A, 1992.

**Anstadt MP**, Tedder M, Hendry PJ, Lowe JE: *Myocardial Function Following Successful Cardiac Resuscitation with Mechanical Circulatory Support*. Critical Care Medicine 20(4):S86,1992.

**Anstadt MP**, Griffith RF, Hoekstra J, Anstadt GL, Brown CG: *Acute Myocardial Reperfusion Using Direct Mechanical Ventricular Actuation vs. Hand Cardiac Massage*. Critical Care Medicine 20(4):S25,1992.

**Anstadt MP**, Hendry PJ, Plunkett MD, Tedder M, Tamayo A, Lowe JE: *Pulsatile vs. Nonpulsatile Flow: Hemodynamics and Organ Perfusion During Resuscitative Circulatory Support*. The 38th Annual Meeting of ASAIO, Abstract Book 21:37,1992.

**Anstadt MP**, Tedder M, Hendry PJ, Plunkett MD, Hegde S, Lowe JE: *Ischemic Preconditioning Results from Severe Global Myocardial Ischemia*. The 38th Annual Meeting of ASAIO, Abstract Book 21:37,1992.

**Anstadt MP**, Tedder M, Hegde S, Sperling R, Lowe JE: *Intraoperative Timing May Predict Thresholds for Assist Device Utilization*. The 38th Annual Meeting of ASAIO, Abstract Book 21:54,1992.

Tedder M, Wharton JM, **Anstadt MP**, Revishvili AS, Hegde SS, Lowe JE: *Optimal Defibrillator Patch Configurations Include the Right Heart and Left Ventricle*. NASPE 15(4), Part II:565, 1992.

**Anstadt MP**, Banit D, Perez-Tamayo RA, Chen F, Abdel-aleem S, Anstadt GL, Lowe JE: *Non-Blood Contacting Circulatory Support After CABG does not Impair Graft Flow*. Presented at the 39th Annual ASAIO Meeting, 1993.

Perez-Tamayo RA, **Anstadt MP**, Walthall HP, St. Louis JA, Wurzel D, Anstadt GL, Lowe JE: *In-Vitro Analysis of Cardiac Actuation*. Presented at the 39th Annual ASAIO Meeting, 1993.

Abdel-aleem S, Li X, **Anstadt MP**, Perez-Tamayo RA, Lowe JE: *The Stimulation of Glucose Utilization in Myocytes via the Regulation of Fatty Acid Metabolism*. Presented at the 42nd Annual Meeting of the American College of Cardiology, 1993.

Abdel-aleem S, Badr M, **Anstadt MP**, Perez-Tamayo RA, Li X, Lowe JE: *Stimulation of the Insulin-Sensitive Glucose Transporters by 4-BCA in Rat Myocytes*. Presented at the Annual FASEB Meeting, 1993.

Idriss SF, **Anstadt MP**, Anstadt GL, Ideker RE: *Cardiac Compression Improves Defibrillation Efficacy*. Presented at the 66th Scientific Abstract # 3188, Circulation (Suppl I) 88 (4): I-593, Oct 1993.

**Anstadt MP**, Tedder M, Banit DM, Crain BJ, Perez-Tamayo RA, Abdel-aleem S, Lowe JE: *Pulsatile Flow Attenuates Cerebral Reperfusion Injury*. Abstract # 0905, Circulation (Suppl I)88(4): I-170, Oct 1993.

Plunkett MD, Hendry PJ, **Anstadt MP**, Fontana GP, Comporesi EM, Amato MT, Lowe JE: *Chronic Hypoxemia Induces Adaptive Changes in the Neonatal Myocardium*. Presented at the Annual Meeting of the Association of Academic Surgeons, 1993.

**Anstadt MP**, Perez-Tamayo RA, Banit DM, Walthall HP, Chen F, Abdel-aleem S, Reimer KA, Lowe JE: *Direct Mechanical Ventricular Actuation vs. Continued Cardiopulmonary Bypass for Postcardiotomy Circulatory Support Following CABG*. Presented at the 30th Annual Meeting of The Society of Thoracic Surgeons, Jan 31-Feb 2, 1994.

Idriss SF, **Anstadt MP**, Anstadt GL, Lowe JE, Ideker RE: *Cardiac Blood Volume and Geometry Influence Upper Limit of Vulnerability and its Relationship to Defibrillation Threshold*. Presented at the American College of Cardiology 43rd Annual Scientific Sessions, 1994.

**Anstadt MP**, Perez-Tamayo RA, Banit DM, Walthall HP, Cothran RL, Abdel-aleem S, Lowe JE: *Cardiac Tolerance to Mechanical Actuation is Affected by Biomaterial Characteristics*. Presented at the 40th Annual Meeting of The American Society for Artificial Internal Organs, April 1994.

Perez-Tamayo RA, **Anstadt MP**, Cothran RL, Lowe M, Walthall HP, Anstadt GL, Lowe JE: *Prolonged Total Circulatory Support With Direct Mechanical Ventricular Actuation: An Ovine Model*. ASAIO 1995,(Supp)41,(1),36.

**Anstadt MP**, Perez-Tamayo RA, Davies MG, Hagen P-O, Walthall HP, St. Louis JS, Hendrickson SC, Abdel-aleem S, Anstadt GL, Lowe JE: *Aorta-coronary Saphenous Vein Graft Function After Mechanical Cardiac Massage*. ASAIO 1995, (Supp)41,(1), 19.

**Anstadt MP**, Perez-Tamayo RA, St.-Louis JS, Van Trigt P, Lowe JE, Anstadt GL: *Clinical Experience with the Anstadt Cup for Non-Blood Contacting Cardiac Support*. ASAIO 1996,42,(2), 42.

Perez-Tamayo RA, **Anstadt MP**, Stafford, Reiseinger RJ, Ybarra G, McElhaney JE, Lowe JE. *Hemodynamic Analysis of Direct Mechanical Ventricular Actuation*. ASAIO, 1996;42(2), 43.

Perez-Tamayo RA, **Anstadt MP**, Ybarra G, Stafford N, Reisinger R, McElhaney JH, Anstadt GL. *Analysis of External Ventricular Actuation*. ASAIO, 1999;45(2),165.

**Anstadt MP**, Ferguson, Musher DM, Miller CC, Soltero E, Beall AC: *Do Less Invasive Strategies Delay Optimal Treatment of Empyema Thoracis?* CHEST, 1999;116(4),Supp 2,256S.

**Anstadt, MP**, Guill CK, Carwile J, Soltero E, Kroll M, Lucci A, Moake J: *Can the Risk for Recurrent Thrombotic Thrombocytopenic Purpura be Predicted Pre-Operatively?* Presented at the 52<sup>nd</sup> Annual Meeting of the Southwestern Surgical Congress, April 9-12, 2000, Colorado Springs, Colorado.

Anderson JE, Chang, Itani KMF, **Anstadt MP**: *Arteriovenous Graft Complications in a Cohort of 150 patients on Chronic Hemodialysis*. Presented at the 52<sup>nd</sup> Annual Meeting of the Southwestern Surgical Congress, April 9-12, 2000, in Colorado Springs, Colorado.

Feagins LA, Guill CK, Malone JP, Anstadt GL, Nolan DJ, **Anstadt MP**: *Myocardial Dynamics During Direct Mechanical Ventricular Actuation of the Fibrillating Heart*. ASAIO, 2000;46(2), P168.

**Anstadt MP**, Eldin KW, Gordon HS, Krishnan B, Kuebler MK, Soltero E, Green LK: *Is Basaloid Lung Carcinoma a Rare and Highly Aggressive Variant of Non-Small Cell Lung Cancer?* CHEST, 2000;1118,(4), Supp.

Schulte-Eistrup SA, Nonaka K, Tenderich G, Mirow N, El-Banayosy A, Minami K, Nose Y, Koerfer R and **Anstadt MP**: *RV and LV Dynamics During Direct Mechanical Ventricular Actuation of the Failing Heart*. ASAIO, 2001;42, No 2.

Schulte-Eistrup SA, Tenderich G, Amin Parsa MH, Mirow N, El-Banayosy A, Minami K, Nose Y, Koerfer R and **Anstadt MP**: *Direct Mechanical Ventricular Actuation Reverses Cardiogenic Shock in Severely Failing Bovine Heart Model*.

Presented at the 13<sup>th</sup> World Congress of the International Society for Artificial Organs, November 2001.

**Anstadt MP**, Eldin KW, Gordon HS, Pennathur A, Krishnan B, Kuebeler MK, Soltero Emergency Room, Green LK: *Basal Cell Carcinoma Does Not Negatively Impact Prognosis Following Surgical Resection of Non-Small Cell Lung Cancer*. Am J of Respiratory and Critical Care Medicine; 165(8), pA149, April 2002.

Portik-Dobos V, Hutchinson J, Bannan M, Mawulawde K, **Anstadt MP**, Ergul A: *Evidence for Decreased Synthesis and Activity of the Vacular Matrix Metalloproteinase Induction/Activation System in Diabetes*. Presented at the American Diabetes Association Annual Meeting, 2002.

Reddy VB, **Anstadt MP**, Molero M, Fuchs L: *Venous Contraction To Endothelin 1 In Congestive Heart Failure*. J Am Coll of Surg; 195(3), p S17, Sept 2002.

**Anstadt MP**, Portik-Dobos V, Hutchinson J, Bannan M, Ergul A: *Decreased Expression of Matrix Metalloproteinase Inducer and Activator Proteins in Hypertension: Relation to Vascular Remodeling*. Presented at the AHA High Blood Pressure Council Meeting, Sept 22, 2002.

**Anstadt MP**, Franga DL, Portik-Dobos V, Hutchinson J, Bannan M, Mawulawde K, Ergul A: *Matrix Metalloproteinase Expression in CABG Conduits May Explain Increased Stenosis Rates in Venous v. Arterial Conduits*. Presented at the 68<sup>th</sup> Annual International Scientific Assembly of the American College of Chest Physicians, San Diego, Nov 2002.

Franga DL, Yuan J, El-Ramace A, Caldwell R, Caldwell W, Wicker DL, Ergul A, **Anstadt MP**: *Cellular Apoptosis Does Not Increase with Non-Blood Contacting Biventricular Support*. Presented at the Southeastern Surgical Congress, Savannah, GA, Feb 2003.

Franga DL, Wicker DL, White S, Yuan J, El-Ramace A, Caldwell W, **Anstadt MP**: *Direct Cardiac Compression Attenuates Myocardial Stress and Injury in the Acutely Failing Heart*. J Am Coll of Surg, Vol 197(3), pS25, Sept 2003.

**Anstadt MP**, Franga D, Caldwell W, Ergul A: *Mechanical Cardiac Actuation of the Failing Heart Reduces Matrix Metalloproteinases Activity*. ASAIO, 2006;52(2), 61A.

Wozniak CJ, Campbell AM, Gargac SM, Darner RJ, **Anstadt MP**: *Non-blood Contacting Biventricular Mechanical Actuation of the Failing Heart*. Presented at the AATS/Cleveland Clinic Kaufman Symposium of 21<sup>st</sup> Century Treatment of Heart Failure, October 2006.

Wozniak CJ, Pothoulakis AJ, Gargac SM, Darner RJ, **Anstadt MP**: *Velocity Vector Imaging Characterizes Systolic and Diastolic Augmentation of the Failing Heart During Non-Blood Contacting Ventricular Actuation*. JACC, 2007;49(9),supp 1,70A.

Wozniak CJ, Gargac SM, Pothoulakis AJ, Prochaska LJ, Darner RJ, Kerns S, Budharaju S, **Anstadt MP**: *Non-blood contacting Mechanical Support of the Pediatric Failing Heart*. Presented at the Third International Conference on Pediatric Mechanical Circulatory Support Systems and Pediatric Cardiopulmonary Perfusion Annual Meeting, Hershey, PA, May 2007.

Wozniak CJ, Pothoulakis AJ, Gargac SM, Darner RJ, **Anstadt MP**: *Utility of Velocity Vector Imaging in the Assessment of Cardiac Function in the Normal and Failing Heart*. Presented at the 18<sup>th</sup> Annual Scientific Sessions of the American Society of Echocardiography, Seattle, WA, June, 2007.

Wozniak CJ, Pothoulakis AJ, Gargac SM, Darner RJ, **Anstadt MP**. *Echocardiographic Assessment of Direct Mechanical Ventricular Actuation*. ASAIO, 2007;53(2),40A.

Bah CM, Prochaska LJ, Pothoulakis AJ, Wozniak CJ, Gargac SM, Budharaju S, Darner RJ, Kerns S, **Anstadt MP**: *Non-blood Contacting Cardiac Actuation Attenuates Right Ventricular Proapoptotic Signaling in the Acutely Failing Heart*. Presented at the AATS/Cleveland Clinic Kaufman Symposium of 21<sup>st</sup> Century Treatment of Heart Failure, October 2007.

**Anstadt MP**, Budharaju S, Wozniak CJ, Darner RJ, Prochaska LJ, Kerns SA, Gargac SM, Pothoulakis AJ: *Diastolic*

*Augmentation During Direct Mechanical Cardiac Actuation.* ASAIO, 2008;54(2),32A.

Wozniak CJ, Paull DE, Moezzi JE, Scott RP, **Anstadt MP**, York VV, Little AG. *Choice of First Intervention is Related to Outcomes in the Management of Empyema.* Nov 5-8, 2008, Austin, TX.

Budharaju S, Pothoulakis AJ, Kerns SA, Schmitt B, Darner RJ, Prochaska LJ, Portner PM, **Anstadt MP**. *Direct Mechanical Ventricular Actuation Significantly Augments Left Ventricular Function In Failing Rabbit Heart Model.* Circ, 2008;118(18), suppl 2,12.

Budharaju S, Wozniak CJ, Darner RJ, Prochaska LW, Kerns SA, Gargac SM, Pothoulakis AJ, **Anstadt MP**. *Diastolic Augmentation During Direct Mechanical Ventricular Actuation.* Presented at WSU Biomedical Sciences PhD Program Research Retreat, Sinclair Community College 27 May 2009.

**Anstadt MP**, Kerns S, Wozniak CJ, Schmitt BA, Darner RJ, Budharaju S, Prochaska LJ. *Direct Mechanical Ventricular Actuation of the Acutely Failing Heart Attenuates Maladaptive Cell Signaling.* Circulation 2009;120:S1490.

Schmitt BA, Reynolds DB, Troche K, Gallimore JJ, Gargac SM, Darner RJ, and **Anstadt MP**. *Defining Power Specifications for Pediatric Direct Mechanical Ventricular Actuation Systems.* In: 2009 Biomedical Engineering Society Annual Meeting: October 7-10, 2009; Pittsburgh , PA.

Shewale S, Horenziak M, Izu B, Lucot J, **Anstadt MP**, Morris M. *Dilated Cardiomyopathy in Nerve Agent Sarin Treated Mice.* Presented at the American Heart Association High Blood Pressure Research Meeting, September 2010.

Swartzmiller KM, Schmitt BA, Reynolds DB, Perez-Tamayo RA, Darner RJ, **Anstadt MP**. *A Simple Mock Circulatory System for Testing Direct Mechanical Ventricular Actuation.* In: 2010, Biomedical Engineering Society Annual Meeting, Oct 6-9, 2010; Austin, TX.

McConnell PI, Del Rio C, Preston T, Schmidt BA, Darner RJ, **Anstadt MP**. *Short-Term Support via Direct Mechanical Ventricular Actuation Improves Cardiac Function in Chronically Failing Hearts.* Accepted for presentation at Annual Meeting of the International Heart and Lung Society: 11/19/2010.

**Anstadt MP**, Thomas DE, Kathula SK, *Paraneoplastic Cutaneous Leukocytoclastic Vasculitis and Iron Deficiency Anemia as the Presenting Features of Squamous Cell Lung Carcinoma.* J Thor Onc Dec 2010: 5(12):S525.

Swartzmiller KM, Schmitt BA, Reynolds DB, Perez-Tamayo RA, Darner RJ, **Anstadt, MP**. *A Simple Mock Circulatory System For Testing DMVA.* Presented at the 57<sup>th</sup> Annual Conference, ASAIO 2011:57(2) 115.

Schmitt BA, Swartzmiller KM, Reynolds DB, Darner RJ, Perez-Tamayo RA, **Anstadt MP**. *Pneumatic Drive Requirements for Direct Mechanical Ventricular Actuation.* Presented at the 57<sup>th</sup> Annual Conference, ASAIO 2011:57(2) 115.

McConnell PI, Del Rio C, Preston T, Schmidt BA, Darner RJ, **Anstadt MP**. *Short-Term Support Via Direct Mechanical Ventricular Actuation Improves Cardiac Function in Chronically Failing Hearts.* Journal of Heart and Lung Transplantation. April 2011:S49-S49.

Wozniak CJ, Kathula SK, Sarodia BD, **Anstadt MP**. *Lobectomy for Lung Carcinoma with Ipsilateral Pulmonary Artery Agescesis.* Presented at the American Thoracic Society Annual Meeting: May 13-18, 2011.

**Anstadt MP**, Hosta DN, Miller AR, Pence JC. *Recurrent Pleural Effusion as a Late Complication to Ventriculopleural Shunt.* Presented at the American Thoracic Society Annual Meeting: May 13-18, 2011.

Alghamri M, Weir N, Miller J, Zhongyu Y, **Anstadt MP**, Morris M. *Echocardiography Shows Impaired Cardiac Response to Ang II in ACE2 Knockout Mice.* Presented at American Heart Association High Blood Pressure Research Meeting, September 22, 2011.

Iyas S, Ekeh AP, Conley DL, Markert RJ, **Anstadt MP**. *Outcome Following Non-Operative Management in Blunt Aortic Trauma*. Presented at The Society of Thoracic Surgeons 48<sup>th</sup> Annual Meeting, January 28-February 1, 2012.

Schmidt BA, Garvin NJ, Budharaju S, Reynolds DB, Darner RJ, Prochaska LJ, **Anstadt MP**. *Direct Ventricular Compression Improves Mechanical Synchrony of the Acutely Failing Heart*. *Circulation*. 2012. 126:A326.

Metzger SA, Schmitt BA, Carnahan KT, Carver DE, Reynolds DB, **Anstadt MP**. *Novel Use of Ultrasound to Characterize Strain Rates in Mock Heart Ventricles*. Accepted for presentation at the 2013 Biomedical Engineering Society Annual Meeting, Seattle, Washington, September 25-28, 2013.

## PRESENTATIONS

Fifth Congress, International Society for Artificial Organs, Oct. 1985: *Comparison of Closed and Open Chest Cardiac Compression with Direct Mechanical Ventricular Assistance*.

The 29th Annual University Surgical Residents Conference, The Society of University Surgeons, Feb. 1987: *An Improved Method of Internal Cardiac Massage Promotes Salvage of Ischemic Myocardium*.

Thirty-third Annual Meeting, American Association for Artificial Internal Organs, May 1987: *Direct Mechanical Ventricular Assistance Promotes Salvage of Ischemic Myocardium*.

The Society of Thoracic Surgeons, Special Topics in Circulatory Support, Feb. 1988: *Bridge to Cardiac Transplantation Using Prosthetic Biventricular Circulatory Support*.

The 30th Annual University Surgical Residents Conference, The Society of University Surgeons, Feb. 1988: *Angiographic Evaluation of Direct Mechanical Ventricular Assistance*.

Annual Meeting, University Association of Emergency Medicine, May 1988: *Myocardial Hemodynamics Using Direct Mechanical Ventricular Assistance During Ventricular Fibrillation*.

Twenty-fifth Annual Spring Cardiovascular Symposium, Duke University Medical Center, April 1989: *Comparison of Direct Mechanical Ventricular Actuation (DMVA) and Cardiopulmonary Bypass (CPB)*.

Thirty-fifth Annual Meeting, American Association for Artificial Internal Organs, May 1989: *Comparisons of Direct Mechanical Ventricular Actuation (DMVA) and Cardiopulmonary Bypass (CPB)*.

Annual Meeting, University Association of Emergency Medicine, May 1989: *Mechanical Ventricular Assistance Following Fifteen Minutes of Ventricular Fibrillation in a Swine Model*.

62nd Scientific Sessions of American Heart Association, October 1989: *Resuscitation in Humans Using Direct Mechanical Cardiac Actuation*.

62nd Scientific Sessions of American Heart Association, October 1989: *Biventricular Mechanical Cardiac Actuation in Humans*.

31st Annual Meeting of the Society of University Surgeons, Feb. 1990: *Mechanical Cardiac Actuation Achieves Hemodynamics Similar to CPB*.

111th Annual Meeting of the American Surgical Association, April 13, 1991: *Pulsatile Reperfusion Following Cerebral Ischemia Improves Neurologic Outcome*.

37th Annual Meeting of the American Society for Artificial Internal Organs, Chicago, Illinois, April 1991: *Biventricular Cardiac Assist vs. Cardiopulmonary Bypass (CPB) for Resuscitation*.

37th Annual Meeting of the American Society for Artificial Internal Organs, Chicago, Illinois, April 1991: *Lack of Myocardial Trauma Following Acute Biventricular Cardiac Actuation for Resuscitation*.

Third Annual Meeting: The Robert M. Zollinger Ohio State University Surgical Society, May 3-4, 1991: *Direct Mechanical Ventricular Actuation (DMVA) Improves Outcome Following Cardiac Arrest Compared to Cardiopulmonary Bypass.*

Circulatory Support 1991, The Society of Thoracic Surgeons, Nov. 15-17, 1991: *State of the Art Session on Direct Mechanical Ventricular Actuation for Resuscitation.*

Circulatory Support 1991, The Society of Thoracic Surgeons, Nov. 15-17, 1991: *Centrifugal Pump Circulatory Support Following Cardiac Surgery.*

Cardiovascular Science and Technology Conference, December 2-4, 1991: *Investigating Mechanical Actuation of the Heart for Non-Blood Contacting Circulatory Support.*

41st Annual Scientific Session of the American College of Cardiology, Dallas, Texas, and April 12-16, 1992: *Thermodilution Techniques Erroneously Predict Flow Alterations during Cardiac Failure.*

38th Annual Meeting of the American Society for Artificial Internal Organs, Nashville, Tennessee, May 7-9, 1992: *Intraoperative Timing Predicts Thresholds for Assist Device Utilization.*

38th Annual Meeting of the American Society for Artificial Internal Organs, Nashville, Tennessee, May 7-9, 1992: *Clinical Results Using Direct Mechanical Ventricular Actuation.*

38th Annual Meeting of the American Society for Artificial Internal Organs, Nashville, Tennessee, May 7-9, 1992: *Ischemic Preconditioning Results from Severe Global Myocardial Ischemia.*

38th Annual Meeting of the American Society for Artificial Internal Organs, Nashville, Tennessee, May 7-9, 1992: *Pulsatile vs. Non-pulsatile Flow: Hemodynamic and Organ Perfusion during Resuscitative Circulatory Support.*

21st Scientific Symposium of the Society of Critical Care Medicine, San Antonio, Texas, May 25-29, 1992: *Myocardial Function Following Successful Cardiac Resuscitation with Mechanical Circulatory Support.*

21st Scientific Symposium of the Society of Critical Care Medicine, San Antonio, Texas, May 25-29, 1992: *Acute Myocardial Reperfusion Using Direct Mechanical Ventricular Actuation vs. Cardiac Massage.*

29th Annual Meeting of the Society of Thoracic Surgeons, San Antonio, Texas, Jan 25-27, 1993: *Pulsatile Reperfusion Improves Cerebral Flow Compared with Non-pulsatile Reperfusion after Circulatory Arrest.*

Clinical Forum Conference, The American College of Emergency Physicians, Kansas City, KS, April 19-21, 1993: *DMVA for Resuscitation.*

39th Annual Meeting of the American Society for Artificial Internal Organs, April 29-May 1, 1993: *Non-Blood Contacting Circulatory Support After CABG Does Not Impair Graft Flow.*

66th Scientific Sessions of the American Heart Association, Atlanta, Georgia, Nov 8-11, 1993: *Pulsatile Flow Attenuates Cerebral Reperfusion Injury.*

30th Annual Meeting of The Society of Thoracic Surgeons, New Orleans, LA, Jan 31-Feb 2, 1994: *Direct Mechanical Ventricular Actuation vs. Continued Cardio-pulmonary Bypass for Postcardiotomy Circulatory Support Following CABG.*

40th Annual Meeting of the American Society for Artificial Internal Organs, San Francisco, CA, April 13-14, 1994: *Cardiac Tolerance to Mechanical Actuation is Affected by Biomaterial Characteristics.*

Cardiovascular Science and Technology Conference, December 9-11, 1994: *Recent Progress Using the Anstadt Cup for Non-Blood Contacting Circulatory Support.*

41st Annual Meeting of the American Society for Artificial Internal Organs, Chicago, Ill, May 4-6, 1995: *Aorta-coronary Saphenous Vein Graft Function After Mechanical Cardiac Massage.*

42nd Annual Meeting of the American Society for Artificial Internal Organs, Washington, DC, May 2-5, 1996: Panel: *Artificial Organ Use in Emergency Cardiopulmonary Resuscitation - Use of a New Device for Direct Cardiac Compression during Open-Chest Cardiac Resuscitation.*

45th Annual Conference of the American Society for Artificial Internal Organs, San Diego, CA, June 2-5, 1999: *Analysis of External Ventricular Actuation.*

65th Annual Meeting of the American College of Chest Physicians, November 1, 1999: *Do Less Invasive Strategies Delay Optimal Treatment of Empyema Thoracis.*

The 52nd Annual Meeting of the Southwestern Surgical Conference, April 2000: *Can the Risk for Recurrent Thrombotic Thrombocytopenic Purpura be Predicted Preoperatively?*

The 5th International Conference on Circulatory Support Devices for Severe Cardiac Failure, September 15-17, 2000, NY, NY: *Non-Blood Contacting Biventricular Support of the Severely Failing Heart Using Direct Mechanical Ventricular Actuation.*

66th Annual Meeting of the American College of Chest Physicians, October 22, 1999: *Is Basaloid Lung Carcinoma a Rare and Highly Aggressive Variant of Non-Small Cell Lung Cancer?*

Grand Rounds at the German Heart Institute Berlin, September 7, 2001: *Direct Mechanical Ventricular Actuation for Non-Blood Contacting Circulatory Support.*

The 16th Annual Postgraduate Pathology Symposium, The Medical College of Georgia, March 23-24, 2002: *Current Staging Techniques for Non-Small Cell Lung Cancer.*

The 98th International Conference of the American Thoracic Society, May 17-23, 2002: *Basal Cell Carcinoma Does Not Negatively Impact Prognosis Following Surgical Resection of Non-Small Cell Cancer.*

Grand Rounds at Middlesex Hospital, University College London, Sept 13, 2002: *Direct Mechanical Ventricular Actuation for Resuscitative Circulatory Support.*

52nd Annual Conference ASAIO, Chicago, IL, June 7-10, 2006: *Mechanical Cardiac Actuation of the Failing Heart Reduces Matrix Metalloproteinases Activity.*

53<sup>rd</sup> Annual Conference ASAIO, Chicago, IL, June 7-10, 2007: *Echocardiographic Assessment of Direct Mechanical Ventricular Actuation.*

53<sup>rd</sup> Annual Conference ASAIO, Chicago, IL, June 7-10, 2007: Invited lecture. *Development of Non-blood Contacting Pumps.*

The Society of Thoracic Surgeons 45<sup>th</sup> Annual Meeting, Jan 26-28, 2009, San Francisco, CA. Oral presentation, *Non-Blood Contacting Support Device Effectively Augments Myocardial Function of the Neonatal-Sized Failing Heart.*

American Heart Association Resuscitation Science Symposium, Nov 17, 2009: Poster Presentation, #2009-R-13018-AHA. *Direct Mechanical Ventricular Actuation of the Acutely Failing Heart Attenuates Maladaptive Cell Signaling.*

Chicago Multidisciplinary Symposium in Thoracic Oncology, Dec 9-11, 2010, Chicago, IL: Paraneoplastic Cutaneous Leukocytoclastic Vasculitis and Iron Deficiency Anemia as the Presenting Features of Squamous Cell Lung Carcinoma.

American Thoracic Society Annual International Meeting, May 13-18, 2011, Denver, CO: *Lobectomy for Lung Carcinoma with Ipsilateral Pulmonary Artery Agenesis.*

American Thoracic Society Annual International Meeting, May 13-18, 2011, Denver, CO: *Recurrent Pleural Effusion as a Late Complication to Ventriculopleural Shunt.*

Annual American Heart Association Resuscitation Science Symposium, November 4, 2012. Schmidt BA, Garvin NJ, Budharaju S, Reynolds DB, Darner RJ, Prochaska LJ, **Anstadt MP**. *Direct Ventricular Compression Improves Mechanical Synchrony of the Acutely Failing Heart*.

Anstadt, MP *Esophageal Disease in the Geriatric Patient – Presented at the 24<sup>th</sup> Annual Statewide Geriatric Medicine Conference, October 11-13, 2013.*

## PROFESSIONAL CONTINUING EDUCATION COURSES

The Society of Thoracic Surgeons Thoracic Endografting Symposium Intuitive Surgical daVinci Surgical System & EndoWrist Instruments for a Console Surgeon	Aug 26-28, 2005 April 4, 2006
GORE TAG™ Thoracic Endoprostheses Physician Training Program Edwards ONE Basic Endovascular Skills Training Program (BEST) Boston Scientific Endoscopic Radial Artery Harvest Course St. Jude Presentation & Discussion on Atrial Fibrillation Transcatheter Therapy for Structural Cardiovascular Disease	Aug 25, 2006 June 26-27, 2007 July 31, 2007 August 15, 2007 Cleveland Clinic October 4, 2007
Advanced Trauma Life Support Instructor Course, #31263-I Advanced Trauma Life Support Course Instructor, #30873-P Cook Medical Advanced Endovascular AAA Physician Workshop Baylor College of Medicine Sternal Wound Management: New Surgical Strategies Edwards Lifesciences Heart Valve Therapy, Global Mitral Summit Advanced Trauma Life Support Course Instructor, #30873-P Premier Health Partners Physician Leadership Series, Levels I-III, Annual Courses Minimally Invasive Thoracic VATS Course, Los Angeles, CA Society of Thoracic Surgeons, Minimally Invasive Valve Symposium, Chicago, IL	January 17-18, 2008 June 16-17, 2008 June 11-13, 2008 June 14, 2008 June 12-13, 2009 June 17-18, 2009 2007- 2011 Apr 6-10, 2010
Endovascular Mini-Fellowship, Arizona Heart Institute, Phoenix, AZ Synthes Rib Trauma Workshop, Grant Medical Center, Columbus, OH Covidien Minimally Invasive VATS Lobectomy Course, National Harbor, MD Medtronic Endovascular Therapies Peer to Peer Training EVAR, Houston, TX Medtronic Endovascular Therapies Peer to Peer Training TEVAR/EVAR Training, Durham, NC Mini-fellowship in Thoracic VATS, Los Angeles, CA Advanced Thoracic Round-Table Discussion, New Orleans, LA Midwest Valve Symposium, Chicago, Ill Covidien VATS Lobectomy Mini-Fellowship, Los Angeles, CA Summit for Perfusion Imaging and Excellence in Surgery, Las Vegas, NV	Dec. 2-4, 2010 Apr 16-20, 2011 Sept. 17, 2011 Oct. 12-13, 2011 Oct. 29-30, 2012 April 34-25, 2013 August 19-21, 2014 August 15, 2014 June 16-17, 2014 August 19-21, 2014 September 13, 2014

## REFERENCES

George R. Brown, MD  
Cardiothoracic Surgery  
937-371-4111

Mukul S. Chandra, MD  
Miami Valley Cardiologists  
Cardiology  
937-681-0133

Marion F. Brown, MD  
Miami Valley Hospital, Director Surgical Services

Cardiothoracic Surgery  
937-689-1654

Steven L. Chambers, MD  
Pulmonary & Critical Care Consultants  
Pulmonary/Critical Care  
937-271-5699

Syed Najeed, MD  
Dayton Cardiology & Vascular Consultants  
Cardiology  
513-702-5799

Jeffrey Pence, MD  
Dayton Children's Hospital  
Pediatric Surgery  
252-412-2697

Anthony Perez-Tamayo, MD  
Cardiothoracic Surgery  
708-822-3064

Paul F. Heyse, MD  
Miami Valley Heart & Lung Surgeons  
Vascular/General Surgery  
937-475-4255